Studies of anorectal function using high resolution anorectal manometry in health and faecal incontinence

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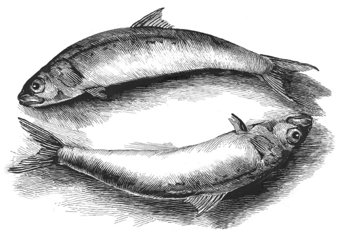
“Life is rather like a tin of sardines - we’re all of us looking for the key”

Alan Bennett

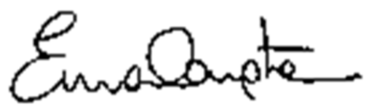


Statement of Originality

The author wishes to certify that all the work presented in this thesis is original in concept, design and execution, although some of the applied techniques have been described previously, or are use in clinical practice. The author performed all the experiments, data acquisition, analysis of the resulting data and preparation of this thesis unless clearly stated otherwise.

In particular, a proportion of data from patients with FI presented in chapters 5, 6 and 7 were performed by members of staff within the Gastrointestinal (GI) Physiology Unit and were not repeated by the author. Design of novel algorithms for analysis of anorectal function were developed in conjunction with a software engineer.

The author was responsible for acquiring appropriate ethical approval, recruitment of volunteers and patients, execution of studies, data inputting and analysis.



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Carrington EV, Brokjaer A, Craven H, Zarate N, Horrocks EJ, Palit S, Jackson W, Duthie GS, Knowles CH, Lunniss PJ, Scott SM. Neurogastroenterol Motil. 2014 May;26(5):625-35

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Abstracts associated with this thesis

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EV Carrington, A Hobson, CH Knowles, PJ Lunniss, SM Scott
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Novel measures of anal function using high-resolution anal manometry (HRAM) outperform conventional manometric measures in female patients with faecal incontinence
EV Carrington, E Tangenberg, A Meek, CH Knowles, SM Scott
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Squeeze profile - a novel and improved measure of anal function using high-resolution anal manometry
EV Carrington, E Tangenberg, EJ Horrocks, S Palit, CH Knowles, SM Scott
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Squeeze profile - a novel and improved measure of anal function using high-resolution anal manometry
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Clinical utility of anorectal manometry for the diagnosis of dyssynergic defaecation: blinded assessment reveals that existing criteria cannot differentiate between patients and controls
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Discordant practice in anal manometry – a survey of physiology departments in the United Kingdom
EV Carrington, M Fox, CH Knowles, SM Scott
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International survey of methods for anorectal manometry: An exploration of variability in current practice
EV Carrington, H Heinrich, M Fox, SS Rao, CH Knowles, SM Scott
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Thesis abstract

Introduction

Faecal incontinence (FI) is a prevalent complaint in Western populations and causes significant disability. Impaired motor function of the anal canal is a common pathophysiological feature and assessment of sphincteric function with manometry is a routine part of symptom assessment.

High-resolution anorectal manometry (HRAM) may provide a more detailed understanding of anorectal function, however its clinical utility has not been established.

Aims

The principal aims of this thesis were to:

(1) Explore existing practices of anorectal manometry
(2) Examine current evidence supporting the use of HRAM
(3) Develop and validate a protocol for the performance of HRAM
(4) Define normal values for traditional measures of sphincteric function using HRAM
(5) Develop and validate novel measures of sphincteric function, and explore whether they improve diagnostic accuracy in patients with FI
(6) Examine anorectal function over a prolonged period with HRAM to evaluate the phenomenon of anal sampling (referred to in this thesis as transient anal sphincter relaxations [TASRs])

Methods

The following methods were used:

(1) A worldwide survey of current practices of anorectal manometry
(2) A systemic review of the literature
(3) Prospective studies (both standard and prolonged) of anal function in healthy volunteers and patients with FI

Results

The practice of anorectal manometry is markedly variable internationally with no two centres surveyed employing the same methods. Within the 62 centres surveyed, there were 16 combinations of ways in which squeeze data were reported. A review of the literature demonstrated a growing evidence base for the use of HRAM however there is a paucity of data that confirm added benefits of HRAM over conventional manometry.

A standardized protocol for HRAM was developed to allow the reporting of traditional measures of anorectal function. Novel measures derived from HRAM were developed which demonstrate increased sensitivity for the detection of impaired sphincteric control in patients with FI (sensitivity of traditional measure [conventional squeeze increment] 36% *vs*. 59% for the novel HRAM measure [5-second squeeze profile]).

Transient anal sphincter relaxations (TASRs) were characterized using HRAM. In health, TASRs are often perceived by the individual as the urge to pass wind (39% of events) and their frequency increases following meal consumption. Conversely in FI, TASRs are a rare occurrence and are generally not perceived (only one patient (1/10 [10%]) with FI reported GI sensations associated with TASR events).

Conclusions

Anorectal manometry is in need of standardization. Novel measures derived from HRAM may improve diagnostic utility and further exploration of TASR characteristics might give insight into the pathophysiology of FI.

Abbreviations

3D	Two-dimensional
3D	Three-dimensional
3D-HRAM	Three-dimensional high resolution anal manometry
ARM	Anorectal manometry
ANMA	Asian Neurogastroenterology and Motility Society
ANGMA	Australasian Neurogastroenterology and Motility Association
ANMS	American Neurogastroenterology and Motility Society
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
BET	Balloon expulsion time
CAM	Conventional anal manometry
CAM-RA	Conventional anal manometry resting average
CAM-SI	Conventional anal manometry squeeze increment
CI	Confidence interval
DCI	Distal contractile integral
DDV	Defaecatory desire volume

DRE	Digital rectal examination
EAS	External anal sphincter
ENMS	European Neurogastroenterology and Motility Society
FACL	Functional anal canal length
FCS	First constant sensation
FI	Faecal incontinence
GI	Gastrointestinal
HRAM	High resolution anal manometry
HRAM-RA	High resolution anal manometry resting average
HRAM-RP	High resolution anal manometry resting profile
HRAM-SI	High resolution anal manometry squeeze increment
HRAM-SP-5	High resolution anal manometry resting profile (5 seconds)
HRAM-SP-30	High resolution anal manometry squeeze profile (30 seconds)
IAPWG	International Anorectal Physiology Working Group
IAS	Internal anal sphincter
ICC	Intraclass coefficient

IQR	Interquartile range
KESS	Knowles Eccersley Scott Symptom
Hz	Hertz
HV	Healthy volunteer
MHz	Megahertz
mmHg	Millimetres of mercury
MMS	Medical Measurement Systems Inc
MR	Magnetic resonance
MTV	Maximum tolerated volume
PAC-SYM	Patient assessment of constipation – symptoms
PAC-QoL	Patient assessment of constipation – quality of life
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PTNS	Percutaneous tibial nerve stimulation
RAIR	Rectoanal inhibitory reflex
RM-ANOVA	Repeated measures analysis of variance
ROC	Receiver operator curve

Sig.	Significance
SD	Standard deviation
SE	Standard error
SEM	Standard error of the mean
SF-36	Short Form-36
SMR	Sensorimotor response
SNS	Sacral nerve stimulation
SS	Solid-state
TASR	Transient anal sphincter relaxation
Q-Q plot	Quantile-quantile plot
QoL	Quality of life
UK	United Kingdom
VAS	Visual analogue scale
WP	Water-perfused

Table of contents

Index of tables

Index of figures

Chapter 1

1 Introduction: anorectal function, maintenance of continence and description of anorectal manometry

1.1 Anatomy and physiology of the anorectum

1.1.1 Embryological development

Formation of the primitive intestine begins in the 3rd week of gestation and originates secondary to the ventral folding of the embryonic yolk sac. This process results in a tubular structure lined with endoderm (which ultimately forms the colonic mucosa) and covered with mesoderm (from which arises the surrounding muscle and serosa) (Pokorny et al., 1996).

The primitive intestine subsequently develops into foregut, midgut and hindgut regions with the colon and upper rectum derived from the mid- and hind-portions (the midgut spanning from the 2nd part of the duodenum to the middle 3rd of the transverse colon and the hindgut extending from the middle 3rd of the transverse colon to the anorectal junction) (Wexner and Jorge, 2005).

The distal rectum and proximal anus are derived from the endodermal lined cloaca and are well defined by the 3rd week of gestation. By the 6th week, the cloaca has developed into the primary urogenital sinus anteriorly and the anorectum dorsally, separated initially by the urogenital septum, then ultimately by the anal membrane (Godlewski and Prudhomme, 2000).

Once fully formed, the anal canal consists of 2 parts distinct in derivation, vascular supply, innervation and lining. The upper part is derived from the cloaca as described above, and the lower part from embryological fusion of the cloaca with the ectodermal proctodeum (Godlewski and Prudhomme, 2000). The point at which these two structures meet is often referred to as the dentate line.

1.1.2 The rectum

The word rectum is derived from Latin meaning ‘straight’ or ‘regular’ in part due to its appearance in lower mammals. The main functions of the rectum are (1) temporary storage of stool prior to evacuation (2) co-ordination with the anal canal to allow recognition of the need to defaecate and (3) propulsion of contents towards the anal canal during defaecation.

In humans, the rectum appears curved as it follows the inner aspect of the sacrum (Heald and Moran, 1998). It is the continuation of the sigmoid colon and terminates at the anorectal junction after piercing the levator ani to become continuous with the anus.

The arterial supply is derived from the superior rectal artery, a branch of the interior mesenteric artery with venous drainage to the inferior mesenteric vein.

The rectum is covered by the mesorectum, derived from the dorsal mesentery, a structure that has become of prime importance during oncological dissection (Heald et al., 1982, Heald and Ryall, 1986). It is covered with peritoneum anterolaterally in its upper third and anteriorly only in the middle third. It is extraperitoneal in its lower third.

Secretomotor control of rectal function is predominantly autonomic in nature. Inhibitory sympathetic supply originating from the 1st and 2nd lumbar spinal segments is delivered via the lumbar and sacral splanchnic nerves which terminate as the inferior mesenteric and superior / inferior hypogastric plexuses. Secretomotor preganglionic parasympathetic supply is via the pelvic splanchnic nerves, which travel to the rectum via the superior and inferior hypogastric plexuses (Standring, 2008).

Sensory function of the rectum is mediated primarily by pelvic and splanchnic afferents. Three functionally and anatomically distinct groups of receptors exist which each respond to distinctive stimuli. Nerve terminals within the serosa are activated by mesenteric distortion (i.e. vigorous distension), afferents within the muscularis externa respond to more moderate distension and mucosal afferents are sensitive to mechanical (light-touch) deformation of the mucosa (Lynn and Blackshaw, 1999, Berthoud et al., 2004).

1.1.3 The anus

The word 'anus' derives from Latin meaning 'a ring' and is comprised of the anal canal and the encircling anal sphincters. The function of the anus is to control and co-ordinate the expulsion of stool and it is under voluntary and involuntary control.

In the adult, the anus is 3 – 4 cm in length, beginning at the dentate line and ending at the anal verge. It is related posteriorly to the coccyx, puborectalis and the anal sphincters, laterally to the ischorectal fossae, Alcock's canal and the inferior haemorrhoidal vessels and anteriorly to the urogenital triangle in the male and the perineal body in the female (Dunphy, 1948, Goligher et al., 1955, Keighley, 1993a).

1.1.4 The anal canal

The lateral walls of the anal canal are in close contact and in health the anal canal is closed at rest. The anal mucosa is arranged in a series of 6- 12 longitudinal folds known as the 'anal columns ' or 'columns of Morgagni'. These are thought to have a role in continence by providing a physical barrier to the passage of stool (Martin et al., 1986, Wood and Kelly, 1992). More distally the anal columns are joined by folds of mucous membrane and at this point are typically termed the 'anal valves' or 'valves of Ball' (Wood and Kelly, 1992).

This transition point between the columns of Morgagni and the valves of Ball is known as the mucocutaneous junction or the aforementioned dentate line. The mucosa is columnar proximal to this and squamous distally.

The anal canal has a dense sensory innervation provided by a combination of free and organized nerve endings. Such apparatus include Meissner corpuscles (sensitive to light touch), Krause end-bulbs (thermoception), Golgi-Mazzoni bodies / lamellar (vibration), and genital corpuscles (vibration and light touch) (Duthie and Gairns, 1960).

1.1.5 The anal sphincters

The anal sphincter was first described by Vesalius, in the 16th century in *De humani corporis* (Versalius, 1555). This sphincter complex can be subdivided into the external anal sphincter, internal anal sphincter and longitudinal muscle (Keighley, 1993a).

The external anal sphincter (EAS) is a striated muscle that encircles the anal canal. It is under voluntary control and has a type I (slow twitch) fibre predominance (Beersiek et al., 1979). Innervation is supplied by neurons originating in Onuf's nucleus carried through the inferior rectal nerves and subsequent right and left pudendal nerves (Bharucha, 2006a).

Despite a wealth of literature published on the subject, there has been much disagreement over the description of EAS anatomy (Schuster, 1975). It has been described as consisting of between 1 – 3 parts (Milligan and Morgan, 1934, Oh and Kark, 1972, Dalley, 1987) though more recent studies, both histological and radiological, suggests a composition of 2 distinct zones (subcutaneous and superficial) separated by a layer of connective tissue (Peschers et al., 1997, Stoker et al., 2001). Though principally cylindrical, radiological studies have demonstrated that this muscle is significantly thicker and shorter posteriorly in its craniocaudal aspect than anteriorly (Fenner et al., 1998, Raizada and Mittal, 2008).

The internal anal sphincter (IAS) is a continuation of the circular smooth muscle of the rectum and is visceral in origin (Wood and Kelly, 1992). It extends from the anorectal ring to approximately 1.5cm below the dentate line and is traversed by fibres of the longitudinal muscle and the anal glands (Sangwan and Solla, 1998). Radiological studies suggest that the thickness of this muscle is about 2 – 3 mm in health (Burnett and Bartram, 1991).

The IAS is composed of composed of slow-twitch, fatigue-resistant smooth muscle fibres and it displays tonic activity at rest (Frenckner, 1975). This activity is modulated by autonomic innervation from both the sympathetic hypogastric and the sacral parasympathetic plexuses (Wood and Kelly, 1992) and provocational studies suggest that the IAS is responsible for between 55 - 85% of baseline anal pressure (Frenckner and Euler, 1975, Lestar et al., 1989).

Although difficult to visualize macroscopically, examination of anatomic sections have confirmed the presence of a third component of the sphincter complex, the longitudinal muscle (Konerding et al., 1999). This is thought to be a continuation of the longitudinal layer of the rectal musculature and is composed of smooth muscle fibres that intersect those from the internal anal sphincter.

Although, not intrinsically part of the anal canal *per se*, the puborectalis is physically and functionally related to the anal sphincters and therefore deserves specific mention. A muscular sling that originates from, and attaches to the pubis anteriorly, it wraps around the rectum posteriorly with the resultant traction maintaining the anorectal angle. It is composed of both type I and type II fibers and is innervated directly from sacral segments II–IV and under voluntary and reflex (sacral outflow) control (Azpiroz et al., 2005).

1.2 The physiology of defaecation and continence

It is well appreciated that evacuatory control is a function of the combined activities of the colon, rectum and anus. Defaecation can be described in terms of four discrete physiological phases: (1) the basal phase characterised by phasic colorectal propulsive activity (2) the pre-defaecatory phase characterised by arrival and recognition of stool in the rectum (3) the expulsive phase during which evacuation occurs and (4) termination of defaecation (Palit et al., 2012).

The contribution of the sensorimotor functions of the colon, rectum and anus to each of these phases are considered separately below.

1.2.1 Colonic function

Colonic motor function is characterised by the mixing and propulsive movements of the colon that allow for digestion, absorption and transit of intraluminal contents. The mechanisms responsible for absorption in the colon are slow and colonic microflora are facilitated by the speed and orientation of mixing movements. Distal propulsion of contents is therefore gradual to allow for mixing and uniform contact with the colonic mucosa. Contents take up to 30 hours to traverse the length of the colon, compared to 2-4 hours in the small bowel (which is four or five times greater in length) (Carrington and Scott, 2014).

Colonic motility patterns are complex and coordinated activity between the terminal ileum, caecum and proximal colon is required to deliver chyme from the terminal small bowel to the large bowel (Karaus and Wienbeck, 1988). Contents become increasingly solid as water is absorbed are transported aborally toward the rectum for eventual evacuation (Scott, 2003).

Antegrade movement of colonic contents is generally a result of proximally originating propagatory pressure sequences (Dinning et al., 2008). The frequency of these pressure sequences significantly increases after waking or meal ingestion and may be of high (associated with a > 100mmHg rise in colonic pressure over a significant length of bowel) or low amplitude (2 – 5 mmHg increase in pressure). Approximately 1 hour prior to the act of defaecation, the frequency and amplitude of antegrade contractions increases throughout the whole colon (Bampton et al., 2000) signaling the beginning of the pre-defaecatory phase.

In health, the propagatory pressure sequences have been shown, to some extent, to be related to the urge to defaecate (Bampton et al., 2001). This is thought to be secondary to movement of colonic contents into the rectum resulting in activation of rectal mechanoreceptors and a sense of rectal filling (Bampton et al., 2000).

1.2.2 Rectal function

The primary role of the rectum is as a temporary storage vessel for stool prior to the onset of defaecation. That being said, the rectum is generally empty during the basal phase of defaecation and its motor activity until the pre-defaecatory phase is mostly characterised by retrograde pressure sequences (thought to act as a braking mechanism particularly during sleep) for regulation of stool transport further towards the anal canal (Rao and Welcher, 1996).

During the pre-defaecatory phase in health, rectal filling results in the urge to defaecate (often felt as a fullness in the perineum or presacral area) (Goligher and Hughes, 1951a). The origin of this sensation is somewhat debated (Womack and Williams, 1988). It was originally believed that this was secondary to stimulation of receptors within the rectal wall, however studies in patients who have previously undergone a rectal resection also report similar sensations of urge (Simonsen et al., 1976, Lane and Parks, 1977) suggesting an extra-rectal location of stimulation.

This sensory urge or 'call to stool' appears fundamental to continence with both heightened and blunted rectal sensitivity associated with disordered defaecation (Chan et al., 2005b, Gladman et al., 2006, Gladman et al., 2009). It has been shown in health that habitual suppression of the desire to defaecate can alter frequency of bowel movements (Klauser et al., 1990). The perception of rectal filling has been demonstrated to be secondary to activation of mechano-sensitive nociceptors that respond to circumferential wall strain (Petersen et al., 2003) and not (as previously presumed) changes in intra-rectal pressure.

The onset of filling results in reflex rectal contraction, another key feature in the maintenance of continence. Aberrant in rectal sensorimotor function resulting in a reduction of rectal compliance has been shown to be particularly present in patients with urge faecal incontinence (Rasmussen et al., 1990, Chan et al., 2005a).

This alteration in rectal wall characteristics is thought to be the stimulus that provokes the intermittent relaxation of the anal canal. This process of 'anal sampling' is thought to be a mechanism for the fine discrimination of rectal contents (Duthie and Bennett, 1963). Reflex relaxation of the internal anal sphincter allows stool to come into contact with the upper anal canal, the epithelium of which contains a diverse range of receptors sensitive to light touch, pain, heat and cold (Duthie and Gairns, 1960). Experimental provocation of this phenomenon is commonly performed during routine anorectal physiology assessment with anorectal manometry and is known as the recto-anal inhibitory reflex (RAIR).

1.2.3 Anal function

It is appreciated that the combined actions of puborectalis and the anal sphincters result in the final physical barrier to the leakage of stool. In addition, the reflex action of the IAS is thought to play an important role in the instigation of defaecation.

The puborectalis sling is central to both effective evacuation and the maintenance of continence (Tagart, 1966, Azpiroz et al., 2005). At rest it forms an acute angle between the posterior rectum and the anal canal which becomes more acute during voluntary squeeze and cough (Parks, 1975). Initial reports suggested that this ‘flap valve’ effect might be a continence control mechanism and resulted in a series of studies that demonstrated some restoration of continence through repair of the anal sphincters with alteration of puborectalis morphology (Womack et al., 1988, Miller et al., 1989b).

More recent studies of the properties of puborectalis have confirmed notable differences between continent and incontinent individuals. In particular, investigation with dynamic MRI suggests that incontinence is highly associated with puborectalis atrophy (Bharucha et al., 2005). Additionally patients with incontinence have been shown to have impaired puborectalis contraction force, a finding that was related inversely with clinical severity (Fernandez-Fraga et al., 2002).

The IAS has a high degree of tone at rest and as such is responsible for up to 85% of baseline anal sphincter pressure (Frenckner and Euler, 1975). IAS activity is reflexly inhibited by mechanical distension the rectum and results in a generalized reduction in anal sphincter pressure (Gowers, 1877, Denny-Browne and Robertson, 1935, Cheeney et al., 2012). This neurogenic response is elicited by stimulation of the rectal myenteric plexus and is thought to be the mechanism for the previously described anal sampling (Schuster et al., 1963, Burleigh, 1992).

The EAS is a voluntary muscle with some tonic activity at rest. Its type I fibre predominance means that voluntary contraction cannot be maintained due to fatigue and it is therefore thought of as the final barrier to evacuatory control (Keighley, 1993b). It is known to respond to rectal filling through the pudendal mediated recto-anal contractile response, presumably to avoid the inadvertent passage of stool (Goligher and Hughes, 1951b, Ihre, 1974, Womack and Williams, 1988).

Disruption of the anal sphincters (commonly secondary to obstetric injury in females and anal surgery in males) is appreciated to be strongly associated with altered continence and sphincter function is known to worsen with age (Parks, 1975, Poos et al., 1986, McHugh and Diamant, 1987, Keighley, 1993b, Jameson et al., 1994, Kamm, 1994, Ryhammer et al., 1997, Rao, 2004, Lunniss et al., 2004, Kim et al., 2008, Boyle et al., 2012). This is further explored in section 1.3.2 below.

1.3 Faecal incontinence

Faecal incontinence occurs when there is disruption of the normal anatomy or physiology of the anorectal unit (Rao, 2004). The term FI is used to describe a wide range of symptoms, from occasional and predictable soiling with stool to the frequent and unpredictable involuntary loss of entire bowel motions.

The Rome III foundation describes functional faecal incontinence as 'the recurrent (symptom duration >3 months), uncontrolled passage of faecal material in an individual with a developmental age of at least 4 years' in the presence of one or more of the following diagnostic criteria (Bharucha et al., 2006a):

(1) Abnormal functioning of normally innervated and structurally intact muscles
(2) Minor abnormalities of sphincter structure and/or innervation
(3) Normal or disordered bowel habits, (i.e., fecal retention or diarrhea)
(4) Psychological causes

This definition requires the exclusion of:

(1) Abnormal innervation caused by lesion(s) within the brain (e.g., dementia), spinal cord, or sacral nerve roots, or mixed lesions (e.g., multiple sclerosis), or as part of a generalized peripheral or autonomic neuropathy (e.g., due to diabetes)
(2) Anal sphincter abnormalities associated with a multisystem disease (e.g., scleroderma)

(3) Structural or neurogenic abnormalities believed to be the major or primary cause of faecal incontinence

1.3.1 Epidemiology

Varying degrees of FI are reported by approximately 1-15% of UK adults outside nursing institutions (Perry et al., 2002, Nelson, 2004) when allowing for under-reporting as only 15-45% seek treatment (Johanson and Lafferty, 1996, Edwards and Jones, 2001). For this reason faecal incontinence is often dubbed 'the silent affliction' (Johanson and Lafferty, 1996).

The most recent survey in non-institutionalized adults living in the United States found the prevalence of FI to be approximately 8.4%, with symptoms equally prevalent in females and males (8.9% *vs.* 7.7%; p = 0.31). Approximately ¼ of these individuals report that symptoms occur more than once per week (2.8% of females and 2.6% of males) and 0.9% of individuals report symptoms occurring more than once per day. In addition, there is an increased prevalence of FI with age with symptoms present in 2.6% of individuals at 20-29 years of age and 15.3% of individuals aged over 70 (Whitehead et al., 2009b).

This finding of an increased prevalence of FI with age (Edwards and Jones, 2001, Perry et al., 2002) is particularly pertinent in modern society, as FI will likely become a greater problem in an increasingly aging population.

1.3.2 Pathophysiology

Epidemiological studies have identified a number of risk factors for the development of faecal incontinence including increasing age, elevated body mass index, co-existent urinary incontinence, history of diabetes, stroke or osteoarthritis, and the use of psychoactive medications (Quander et al., 2005, Alimohammadian et al., 2014).

Specific pathophysiological mechanisms underlying FI are often broadly divided into abnormalities of anorectal structure, function or unfavorable stool characteristics and are shown in Table 1-I.

Category		Cause	Resultant mechanistic effect
Structure	Anal sphincter	Obstetric injury Iatrogenic (e.g. surgucal)	Poor sphincter function
	Rectum	Inflammation Radiation Trauma (e.g.prolapse) Aging	Loss of accommodation
	Puborectalis	Excessive perineal descent Trauma	Obtuse anorectal angle Poor sphincteric function
	Pudendal nerves	Obstetric injury Iatrogenic (e.g. surgucal)	Poor sphincter function Anal hyposensitivity
	CNS	Spinal cord / head injury Trauma Multiple sclerosis, stroke, Diabetes	Impaired anorectal reflexes Abnormal anorectal senstivity Loss of accommodation
Function	Anorectal sensation	Obstetric injury CNS injury	Loss of stool awareness Rectoanal agnosia
	Faecal impaction	Pelvic floor dyssynergia	Faecal overflow Megarectum Abnormal rectal sensitivity
Stool characteristics	loose consistency	Infection IBD IBS Drugs / medications Bile sats	Rectal irritation / faecal urgency Rapid stool transport
	hard consistency	Prolonged colonic transit Drugs / medications	
Miscellaneous	Behavioural	Aging, dementia, disability Willful soiling	Multifactorial changes
	Medications	Anticholiergics Antidepressants Caffine / muscle relaxants	Constipation and faecal overflow Altered colorectal sensation Altered sphincter tone

Table 1-I Pathophysiological mechanisms leading to symptoms of faecal incontinence. Modified from (Rao, 2004).

Within this, obstetric injury is the most often cited aetiological factor for symptom development (Fynes et al., 1999, Rao, 2004, Damon et al., 2006) as it carries risk of damage to the pelvic floor, anal sphincters, and pudendal nerves (Kamm, 1994, Goldberg et al., 2005).

An associated pudendal neuropathy has been found in up to 38% of women with faecal incontinence after vaginal delivery (Fitzpatrick et al., 2003) and primiparous women with symptoms of incontinence experience worsening of symptoms after a repeated childbirth (Fynes et al., 1999). Despite this, symptom onset is typically delayed, with patients presenting 20-30 years following the initial insult (Bharucha et al., 2005).

In men presenting with faecal incontinence iatrogenic injury to the sphincter secondary to anal surgery is a particular risk factor and co-existent benign perianal disease (such as haemorrhoids, fistula-in-ano and radiation proctitis) is common (Kim et al., 2008). It has been demonstrated that up to 59% of males presenting for symptom assessment have previous history of anal surgery (Lunniss et al., 2004).

1.3.3 Clinical presentation

Symptom clusters are seen in faecal incontinence and may allude to the underlying pathophysiological cause. Symptoms are often described as urge or passive related.

Urge faecal incontinence is described as the inability to defer defaecation in the context of a perceived defaecatory desire whereas passive faecal incontinence is the inadvertent loss of stool without warning.

Some efforts have been made to establish whether FI symptoms predict pathophysiology. Indeed, commonly used symptom scoring systems rate the frequency of passive and urge related symptoms separately (Vaizey et al., 1999). Studies of the relationship between symptoms and underlying sphincter defects has demonstrated that passive leakage is associated with abnormal IAS morphology and reduced anal resting pressure, whereas urge incontinence is associated with abnormal EAS morphology and poor voluntary squeeze pressure (Engel et al., 1995).

It should also be appreciated that symptoms of faecal incontinence infrequently appear in isolation. Patients may present with other symptoms of defaecatory dysfunction and there is often co-existence of incontinence symptoms with constipation (most commonly due to overflow leakage with impairment of EAS function or faecal retention and subsequent leakage secondary to pelvic floor dyssynergia) (Read and Abouzekry, 1986, Nurko and Scott, 2011).

Background examination of the history may reveal risk factors for symptom onset such as obstetric injury, pelvic / anorectal surgery, hysterectomy, and may also reveal allied symptoms of other pelvic floor pathology (such as pelvic organ prolapse and urinary incontinence (Green and Soohoo, 1989, Kamm, 1994, Nygaard et al., 1997, Altman et al., 2004, Lunniss et al., 2004, Rao, 2004).

Clinical examination may reveal evidence of previous perineal / perianal injury (either traumatic or iatrogenic), abnormalities or sphincter bulk and control, excessive movement of the pelvic floor and/or altered stool volume/characteristics within the rectum (Keighley, 1993b, Chatoor et al., 2007).

1.3.4 Investigations

As the causes of FI are multifactorial, the primary approach to a patient presenting with symptoms for the first time should be to exclude serious, treatable underlying pathology (such as colorectal malignancy and inflammatory bowel disease) (Norton et al., 2007). Once this has been performed, a decision can be made as to whether further special investigations of continence are warranted (Keighley, 1993b).

There is some argument as to the utility of physiological investigation (Wald, 2006, Bharucha, 2006b, Rao, 2006) and some evidence to suggest that an appropriate amount of pathophysiological information can be gained through clinical history and examination by an experience investigator (Hill et al., 1994). However, evidence to the contrary of this also exists with prospective studies demonstrating that anorectal assessment directly impacts clinical decision-making (Vaizey and Kamm, 2000, Liberman et al., 2001). In addition there is evidence that physiological assessment may provide biomarkers that predict response to treatment (Chiarioni et al., 2002, Altomare et al., 2004, Knowles et al., 2012).

Special investigations of continence generally involve manometric, sensorimotor and neurophysiological assessment of anorectal function. A variety of complimentary investigations are available which are summarized in Table 1-I.

A specific and detailed description of all investigations of anorectal function is beyond the scope of this thesis. A more comprehensive account of anorectal manometry is further described in section 1.4 below.

Structure	Function	Investigation	Clinical use
Colon	motor	radio-opaque marker studies	established
		colonic scintigraphy	research
		colonic manometry	research
Rectum	motor	distal colonic manometry	research
		rectal barostat	established
		rectal motor evoked potentials	research
	sensory	simple balloon distension	established
		rectal barostat	established
		rectal cortical evoked potentials	research
Anorectum	motor & sensory	balloon expulsion	established
		evacuation proctography (fluroscopic)	established
		evacuation proctography (magnetic resonance)	established
		anorectal manometry (conventional)	established
		anorectal manometry (high resolution)	novel
Anus	sensory	electrostimulation	established, though limited use
		thermostimulation	research
		light touch stimulation	established, though limited use
		anal evoked potentials	research
		anocutaneous reflex	established, though limited use
	motor	anorectal manometry (conventional)	established
		anorectal manometry (high resolution)	novel
		electromyography	established, though limited use
	motor & sensory	pudendal nerve terminal motor latencies	established, though limited use
	structure	endoanal ultrasound (two dimensional)	established
		endoanal ultrasound (three dimensional)	established

Table 1-II Table summarising physiological tests available to investigate colonic, rectal and anal function

1.3.5 Conservative management

Initial management of FI generally involves the offer of dietary and lifestyle advice. It is appreciated that in some patients, certain food types may trigger symptoms and many patients report altering their diet to preventing continence. Avoidance of foods that possess naturally occurring laxative effects may have marginal benefit in certain individuals (Bliss et al., 2000).

The next step in management is the use of medications. Most patients with FI will generally receive some form of medical treatment to manage their symptoms. The most typical are anti-diarrhoeal medications such as loperamide and codeine (Hallgren et al., 1994, Sun et al., 1997). In the context of co-existent constipation, treatment with laxatives, suppositories or enemas may be beneficial.

If medications prove ineffective and a motor or sensory deficit is identified, biofeedback can be considered. This is a popular therapy for both rectal sensory dysfunction and pelvic floor dyssynergia however data of effectiveness are mixed (Wald and Tunuguntla, 1984, Buser and Miner, 1986, Miner et al., 1990, Norton et al., 2003, Solomon et al., 2003, Heymen et al., 2009).

Conservative forms of neuromodulation are a recent addition to the armamentarium of therapies available for the treatment of FI. A novel treatment of particular recent interest is percutaneous tibial nerve stimulation (PTNS). Some evidence of clinical effects exists, however data is limited and further prospective studies are required to establish true utility (Govaert et al., 2010, Hotouras et al., 2012, Thin et al., 2013, Grossi et al., 2014, Horrocks et al., 2014).

1.3.6 Surgical management

Following exhaustion of conservative measures, surgical techniques can be considered. These can be conceptually divided into those procedures that (1) recruit / restore residual function (2) restore anatomy or (3) aim to salvage symptoms alone.

Currently, sacral nerve stimulation (SNS) is recommended as the first surgical step for management of idiopathic FI. Direct electrical stimulation of the sacral nerve roots by SNS is a safe, effective, yet less invasive therapeutic option for FI patients failing non-interventional therapies regardless of FI aetiology. It is based on the concept that residual anorectal neuromuscular function pertinent to continence can be recruited by electrical stimulation of its peripheral nerve supply. Review data suggest complete continence following SNS in 41-75%, and > 50% decrease in symptoms in 75-100% of patients (Jarrett et al., 2004, Thin et al., 2013, Horrocks et al., 2014). Sustained functional benefit has been shown to be maintained in the medium term (Matzel et al., 2004), with significant improvements in Quality Of Life (Bharucha et al., 2006b, Hetzer et al., 2006, Hetzer et al., 2007).

The most commonly performed surgical treatment aimed at restoring anatomy is the sphincter repair (Chatoor et al., 2007, Norton et al., 2007). In the short term, sphincter repairs provide good symptomatic benefit (Browning and Motson, 1984, Motson, 1985, Fleshman et al., 1991). Unfortunately long-term outcomes are poor and at 5 years about 50% of patients require further intervention to effect symptom control (Malouf et al., 2000, Bravo Gutierrez et al., 2004).

Other surgical therapies aimed at augmenting anal sphincter function include the dynamic gracilloplasty (Williams et al., 1989, Williams et al., 1990) and the artificial sphincter (Wong et al., 1996, Vaizey et al., 1998a). Due to their invasive nature and the high associated morbidity they are now reserved for patients with intractable symptoms.

The final stage in management is the formation of an end colostomy (Vaizey et al., 1998b, Rao and American College of Gastroenterology Practice Parameters, 2004). This has the advantage of permanently diverting stool in those with intractable and insufferable symptoms however comes with significant social and psychological morbidity.

1.4 Anorectal manometry

Manometry is the method of recording mechanical activity of the gastrointestinal tract through measurement of changes in intraluminal pressure (Gustavsson and Tucker, 1988). As motor control of stool transport is a primary function of the anorectum, manometry is a key investigation for the assessment of patients with evacuatory difficulty (including those with faecal incontinence) (Rao and American College of Gastroenterology Practice Parameters, 2004, Scott and Gladman, 2008). This measurement of intra-anal luminal pressures was first described in 1965 (Duthie and Watts, 1965, Phillips and Edwards, 1965) and is now the most established and commonly performed investigation of anorectal function (Rao, 2004). It's use to determine functional ability of the anal canal and to describe anorectal co-ordination is supported by a number of consensus groups and working parties (Keighley et al., 1989, Barnett et al., 1999, Rao et al., 2002, Drossman DA, 2006).

1.4.1 Types of anorectal manometry

Due to the cylindrical nature of the anal canal and the overlapping orientation of the anal sphincters, two main types of anorectal manometry have emerged; those which measure pressures longitudinally only (e.g. conventional and high resolution anorectal manometry) and those which describe pressures longitudinally and radially.

The development of methods to measure radial anal pressures was first described in 1984 (Taylor et al., 1984) and is known as vector-volume manometry (Schizas et al., 2011). The principle reasoning behind this technique is that the muscular composition of the anal canal is likely to impact radial pressures (Schizas et al., 2016) and asymmetrical sphincter function is likely to reflect underlying sphincter defects (Zbar et al., 1999a). The main quantitative measures typically used to describe this are the Radial asymmetry index (RAI) and the vector volume (Sultan et al., 2016).

In the last 10 years, 9 studies in adults and 3 studies in children have been published describing vector volume manometric analysis. This body of research has demonstrated that pressures within the anal canal vary radially in health (Cali et al., 1992, Williams et al., 1995, Schizas et al., 2011), and this asymmetry may be more profound in patients with incontinence (Williams et al., 1995), particularly in those with sphincteric injury (Sangwan et al., 1996, Fynes et al., 2000).

Unfortunately, to date, few studies of vector volume manometry have compared health and disease states and normative data are lacking with the largest study of healthy volunteers only including 33 subjects (Zbar et al., 1999a). This has resulted in the utility of vector-volume technology to be questioned (Yang and Wexner, 1994, Scott and Gladman, 2008) however vector-volume measurements remains of interest for description of anal function (Sultan et al., 2016) but are currently not part of existing guidelines for routine clinical study of anorectal function (Wald et al., 2014b).

Despite this, there has been particular interest in the development of 3D high-resolution (sometimes referred to as high-definition) catheters with the ability to generate vector-volume data and pilot studies suggest that these data may predict disease status (Rezaie et al., 2016, Zifan et al., 2016).

Vector volume and 3D high-resolution manometry is not available for use within the department associated with this thesis. Therefore, in the remainder of this thesis, vector-volume and 3D descriptions of manometry will not form part of data collection or analysis. However due to the significant potential of radial measurements (Lee et al., 2013, Zifan et al., 2016), published studies utilizing vector volume or 3D high-resolution manometry techniques will continue to be considered.

1.4.2 Technology

All manometry setups consist of two basic components: a pressure sensor / transducer (capable of transforming changes in pressure into an electrical signal) and a recording device which amplifies the data and records it.

Pressure changes can be quantified using water-perfused catheters linked to volume-displacement transducers or solid-state catheters, which use a Wheatstone bridge mechanism to measure strain.

Water perfused systems typically utilise narrow, multi-lumen catheters with a number (usually around 6) of side-opening ports. The openings are distributed typically longitudinally and / or radially around the catheter allowing pressure to be measured simultaneously from a number of positions along the catheter (Read and Sun, 1992). Each lumen is perfused by a low-compliance pneumo-hydraulic pump that slowly drives water through the catheter. Pressures depend on the compliance of the catheter system and the rate of perfusion and are recorded through calculation of the resistance of flow of fluid from the catheter (Murray et al., 2003). Water perfused systems are often employed as they are inexpensive with (usually) disposable catheters however this method has the disadvantage that instillation of water may be uncomfortable to the patient and cause sensory stimulation of the anal canal.

Solid-state catheters use microtransducers to measure strain. Each recording sensor consists of a strain gauge. This strain gauge is formed from a length of fine wire arranged in a grid shape. Resistance of the wire is proportional to its length and inversely proportional to its cross-sectional area. Deformation of this grid changes the resistance of the wire, which is proportional to the strain applied

(Scott, 1998). Solid-state systems are advantageous as they cause less disruption and stimulation of the anorectum (as no water is instilled) however the technology is often criticized due to the increased expense. Recent advances in technology have now resulted in the manufacture of catheters with 16 rows of 16 radially arranged sensors (Sierra Scientific, Los Angeles, CA) over a 6.4cm recording length (Cheeney et al., 2011).

1.4.3 Indications and clinical utility

The utility of and indications for anorectal physiological testing in patients with FI has been discussed in section 1.3.4. Anorectal manometry is the most commonly performed test of anorectal function. Indications for testing are summarized in Table 1-III below.

	Indication
Urgency	Faecal urgency
Incontinence	Urge faecal incontinence Passive faecal leakage Post defaecatory leakage Flatus incontinence
Constipation	Infrequency of stool Evacuatory difficulty
Miscellaneous	Pre-operative sphincter assessment Abdominal pain/bloating Anal pain Post obstetric sphincter assessment Clinical research Baseline functional assessment prior to biofeedback

Table 1-III Indications for anorectal manometry

1.4.4 Performance of anorectal manometry

Despite a number of working party and consensus group recommendations on the subject (Barnett et al., 1999, Azpiroz et al., 2002, Rao et al., 2002), there is no internationally accepted standard protocol for performance of anorectal manometry. The following section describes practices within our unit at the Royal London Hospital. This protocol has recently been adopted by the Association of GI Physiologist (AGIP) section of the British Society of Gastroenterology (BSG) (Association of GI Physiologists, 2013).

Equipment

Either a solid-state (reusable) or water-perfused (usually disposable) high-resolution anal manometry (HRAM) catheter can be used. For water-perfused catheters, perfusion rate is kept to a minimum to limit the volume of water flowing within the anorectum during the procedure, but of sufficient rate to retain fidelity / accuracy of recording. A standard (approximately 6 cm length x 4 cm width; maximum volume >360 ml) non-latex balloon is mounted onto the catheter tip for assessment of rectal sensation and the rectoanal inhibitory reflex (RAIR). If possible, balloon inflation is performed with an automated pump, to allow standardization of inflation speed (for sensation, recommended at 2 ml / min).

Patient selection and preparation in advance of procedure

Patients should be assessed by a gastroenterologist or colorectal surgeon prior to referral for anorectal manometry. Ideally, patients should undergo endoscopy +/- biopsies to exclude carcinoma or inflammatory conditions as the cause of symptoms and to assess for structural abnormalities such as intussusception or stricture. An information leaflet should be given to patients prior to attendance outlining preparation required, what to expect during the procedure, risks and post-procedure advice. Medications that may alter anorectal sensitivity (e.g. morphine) should be avoided unless required for the patient's wellbeing. The patient may continue to take their usual laxatives, enemas or suppositories (if necessary) prior to attendance.

Patient preparation on attendance

The patient may be invited to open their bowels prior to starting the procedure. Enema administration to facilitate rectal emptying is not routinely recommended, although this can be considered in the context of faecal impaction. A full and focused clinical history should be taken from the patient documenting relevant symptoms, associated past medical, surgical / obstetric history and current medications. The procedure explained in detail to allow informed consent and full co-operation during the test. The patient must be given the opportunity to have any questions or concerns they may have answered to their satisfaction before the procedure starts and should be aware of the fact that they can withdraw consent at any time during the procedure. Written consent may be taken, according to local guidelines; however, this can be considered optional, as there are no serious risks associated with the procedure.

Equipment preparation

If reusable, the anorectal catheter should undergo a full cleaning cycle, unless last used and decontaminated within the preceding 3 hours and catheter calibration should be checked as per manufacturers' guidelines. If required, the non-latex balloon should be adequately secured to the catheter, and pre-procedure inflation performed ex vivo to check for air leaks; if present, the balloon should be re-secured to the catheter. If using a solid state system, the catheter should be pre-warmed to body temperature in lukewarm water and zeroed at the start of every procedure (again under 1cm of water).

Performance of the procedure

The member of staff performing the procedure must either be fully trained and accredited in this procedure, or supervised by a fully trained and accredited practitioner. Typically, a chaperone is present during the procedure to offer assistance to the practitioner and to act as a patient advocate.

The patient should be asked to lie down in the left lateral position with a sheet covering any exposed areas to ensure dignity. Firstly, a digital rectal examination should be performed and documented. During digital rectal examination, a brief trial / tutorial of 'squeeze' and 'push' should be performed to ensure patient understanding prior to onset of the procedure.

Lubrication gel should be applied to the catheter prior to commencement of the procedure to allow for comfortable insertion and the catheter tip should be gently advanced through the anus into the rectum. If resistance is felt during insertion, the catheter should be pulled back before re-advancing. If catheter placement is problematic, assessment of catheter kinking can be made digitally. The catheter should not be advanced if discomfort is caused or if placement is overly difficult. If data is to be collected using a stationary technique, the catheter should be placed with at least 1 manometric sensor visible from the anal verge (to facilitate post hoc analysis) and taped into position to prevent inadvertent movement during the testing protocol.

Study protocol

The following manoeuvres are then performed:

- Familiarisation – the patient is asked to lie still, relaxed, without talking if possible. During this time it is useful to mark the limits of the anal canal on the recording equipment for future reference
- Rest – a period of measurement at rest should be performed, again with the patient relaxed and without talking. Any sudden movement (e.g. talking, coughing etc.) should be noted on the trace to prevent confusion during post hoc analysis.
- Squeeze – Squeezes of a standard duration, should be performed in response to the (suggested) following command "please squeeze in tight with the muscles around your bottom and hold until I say stop".
- Endurance squeeze – a 30 second squeeze should be performed in response to the (suggested) following command "please squeeze in tight with the muscles around your bottom. This time I would like you

to hold on for 30 seconds, or as long as you can". The patient should be encouraged to continue squeezing during the 30-second period to aid compliance.

- Push – An attempt to bear down as if to defaecate, should be performed in response to the (suggested) following command "please push / bear down as if you were going to the toilet to open your bowels".
- Cough – two single coughs should be performed, with the patient encouraged to cough as forcefully as possible. The patient should be instructed to refrain from coughing multiple times, as this impairs data interpretation.
- Sensory testing – rectal sensory testing should then be performed, ideally using an automated pump attached to the anorectal catheter. Using a ramp (continuous) inflation paradigm, the balloon should be inflated at a rate of 1-2 ml/second and the patient asked to report: (1) volume for first constant sensation, (2) desire to defaecate volume, and (3) maximum tolerated volume.
- Rectoanal inhibitory reflex (RAIR) – the balloon should be inflated with an automated pump at a rate of 30ml/second to a volume of 60mls. The balloon should then be deflated after a period of 5 seconds. If the reflex is absent, increases in the volumes inflated to 120ml, 180ml, and finally 240ml is undertaken;

Post test procedure

Following the end of the procedure the catheter should be removed and a short period of recording taken ex vivo to ensure there has been no manometric drift. The catheter should then be disconnected for decontamination purposes, and the recording saved for post hoc analysis.

1.4.5 Results analysis

The objectives of anal manometry are:

- To determine the functional anal canal length
- To determine anal canal pressures at rest (commonly accepted as a marker of IAS function)
- To determine anal canal pressures during squeeze (an index of voluntary EAS control)
- To assess rectoanal co-ordination during push

Anal canal length

The functional anal canal length is typically defined as the length over which the anal pressure exceeds the rectal pressure by > 5mmH at rest. It is generally reported in cm (Scott and Gladman, 2008). The anal canal length is shorter in patients with faecal incontinence and sphincteric compromise (Nivatvongs et al., 1981b, Rao et al., 1999).

Anal resting pressure

Anal resting pressure is a result of the combined functions of the IAS and EAS. Experimental studies have demonstrated that the EAS contributes approximately 15% of the total tone of the anal canal (Frenckner, 1975). Pressures within the anal canal undulate secondary to cyclical slow (amplitude 5-25 cmH_20, frequency 6/min) and ultraslow waves (amplitude 30-100 cmH_20, frequency <3/min) (Read and Sun, 1992, Rasmussen, 1994).

Anal resting pressure may be defined as the difference between the intrarectal pressure and the maximum anal sphincter pressure at rest and is often recorded at arbitrary locations within the anal canal (typically at 1, 2, 3, 4 and 5 cm from the anal verge) (Rao et al., 2002, Scott and Gladman, 2008).

Anal squeeze pressure

Anal squeeze pressure is the resultant increase in anal pressure seen during a voluntary squeeze. For squeeze to be successful, the individual has to have a structurally adequate sphincter and the ability to voluntarily control that sphincter on demand (Azpiroz et al., 2002).

Squeeze can be reported in terms of its increment, the absolute pressure reached or the duration of the squeeze sustained (Read and Sun, 1992, Rasmussen, 1994, Azpiroz et al., 2002, Scott and Gladman, 2008). It is essentially a test of voluntary EAS and puborectalis function and poor squeeze increments are seen in patients with FI and sphincteric injury (Enck et al., 1989, Engel et al., 1995, Fynes et al., 1999).

Rectoanal inhibitory reflex

The reflex relaxation of the IAS seen following sudden distension of the rectum is known as anal sampling (Duthie and Bennett, 1963). Experimental provocation of this phenomenon is performed by inflation of a balloon within the rectum (known as the recto-anal inhibitory reflex [RAIR]) (Rao et al., 2002). This reflex may be defined as the transient decrease in resting anal pressure by ≥25% of basal pressure in response to rapid inflation of a rectal balloon with subsequent return to baseline (Lowry et al., 2001).

Reporting of the RAIR typically includes the volume required to elicit the response and may include the duration of the response, the percentage relaxation of response at different volumes and description of the response at different levels of the anal canal (Zbar et al., 1998). Some reports however suggest that a simple 'present/ absent' report may suffice (Azpiroz et al., 2002, Rao et al., 2002, Scott and Gladman, 2008).

Normally, the RAIR consists of an initial increase in anal pressures followed by inhibition of pressures in the proximal anal canal with or without an simultaneous increase of pressures in the distal anal canal (Roberts, 2005). Evidence of alteration in RAIR characteristics in patients with FI when compared to health exists, and subjects may exhibit prolongation of the response, altered responses at different levels of the anal canal or even absence of the response, particularly if there is associated megarectum (Sun et al., 1989, Sangwan and Solla, 1998, Zbar et al., 1998, Kaur et al., 2002, Jung et al., 2014)

The classic absence of a response in Hirschprung's disease (Aaronson and Nixon, 1972) may also be seen however new diagnosis of this disorder in adults is exceptionally rare and usually made on a combination of clinical, radiological and histological grounds.

Push / attempted defaecation

Examination of rectal and anal pressures during the bearing down maneuver allows assessment of voluntary control of the pelvic floor. It is generally accepted that for defaecation to be successful, voluntary effort should result in intra-rectal pressures which sufficiently exceed anal pressures to allow the passage of stool (Rao et al., 1999). Alteration in the recto-anal pressure relationship during this maneuver is observed in patients with symptoms of evacuatory dysfunction (Rao and Patel, 1997, Rao et al., 2004).

The following patterns are seen and may be reported:

a. *normal* – an adequate increase in rectal pressure (≥40mmHg) accompanied by a simultaneous reduction in anal pressure;
b. *type I dyssynergia* – an adequate increase in rectal pressure (≥40mmHg) accompanied by a paradoxical simultaneous increase in anal pressure;
c. *type II dyssynergia* – an inadequate increase in rectal pressure of (<40mmHg) (poor propulsive force) accompanied by a paradoxical simultaneous increase in anal pressure;
d. *type III dyssynergia* – an adequate increase in rectal pressure (≥40mmHg) accompanied by failure of reduction in anal pressure (≤20% baseline pressure);
e. *type IV dyssynergia* – an inadequate increase in rectal pressure of (<40mmHg) (poor propulsive force) accompanied by failure of reduction in anal pressure (≤20% baseline pressure);

1.4.6 Technique limitations

Conventional anorectal manometry suffers from a number of limitations. The first is the limited number of sensors within the anal canal. Only a 'snapshot' of activity is taken at each point in time which leads to difficulty appreciating global anal function (Scott and Gladman, 2008).

Second is the arbitrary nature of reporting pressures at fixed intervals. The functional anal canal length varies between 2.5 – 5cm in its craniocaudal axis in health (Nivatvongs et al., 1981a). Measurement of the anal canal at predefined intervals may lead to failure to recognize areas of maximal activity.

Third is the unidirectional nature of longitudinal only measurement systems. As described previously, it is well appreciated that pressures within the anal canal vary both axially and circumferentially due to activity of the sling-shaped puborectalis (Collins et al., 1969, Raizada et al., 2011). The use of unidirectional sensors and movement of such a catheter within the anal canal is likely to give results that do not necessarily reflect true function (Read and Sun, 1992).

Fourth is the stimulation that manometry causes, especially during the use of water-perfused, pull through techniques. Sensory stimulation of the anal canal will typically cause contraction of the anal canal (either through the anocutaneous reflex or secondary to voluntary activity) and may well impact on absolute values (Sun and Read, 1989).

The final most important limitation of anorectal manometry is the lack of uniformity in performance protocol and results reporting between centres. This is despite several working party statements on the topic (Barnett et al., 1999, Keighley et al., 1989, Azpiroz et al., 2002, Rao et al., 2002). Many of these have failed due to the lack of validation data leaving local centres to develop institution specific practices and local normal ranges, a practice that has undeniably lead to difficulties in results transfer between centres (Scott and Gladman, 2008).

1.4.7 High resolution manometry

The last decade has seen the development of high-resolution anal manometry (HRAM) with key improvements being an increased number of closely spaced microtransducers greatly enhancing spatial resolution; the ability to measure pressure changes circumferentially; and software development to allow novel methods of data analysis and display.

Clouse and Staniano first introduced this ‘high resolution’ method of acquisition and analysis in the early 1990’s for the investigation of the upper gastrointestinal tract. Data pertaining to sensor position, average pressure and time were transformed into pseudo-3D topographic plots to better illustrate functional anatomy of the oesophagus (Miller et al., 1988b, Cornes et al., 1991).

Since then, high-resolution manometry has been demonstrated to significantly improve yield and diagnostic accuracy of oesophageal dysfunction when compared to conventional manometry (Fox et al., 2004, Hansen et al., 2006) and is now the gold-standard method for data acquisition and analysis (Bredenoord et al., 2012).

Application of high-resolution manometry to the anorectum is more recent with the first study detailing its use published in 2007 (Jones et al., 2007). A recent increase in interest has provoked the production of a number of high-resolution systems available for use in both clinical and research settings. These include 2-dimensional systems, which utilise data from a catheter that typically houses between 8 – 12 longitudinal sensors (Carrington et al., 2014a), and 3-dimensional systems, which collect and individually report data from sensors placed not only longitudinally but also radially (Cheeney et al., 2012) and which use descriptive measures similar to that seen with vector volume manometry.

HRAM is likely to offer benefits over convention anal manometry, as it is likely to offer solutions to many of the limitations outlined in section 1.4.6 above. A detailed presentation of the clinical data available for HRAM will be presented in the form of a systematic review in Chapter 3 of this thesis.

1.5 Summary

The maintenance of continence is reliant on the coordinated actions of the colon, rectum and anus. The anorectum is a dynamic and responsive functional unit, able to respond to both visceral and somatic stimuli.

The anal canal in particular is richly innervated with a variety of sensory receptors, however its exact role in the perception of defaecatory urge remains poorly understood. It is thought that the synchronization of anorectal motor and sensory function may be implicated in this through the process of anal sampling, however this reflex has been largely unexplored with modern methodological techniques.

Faecal incontinence (FI) is a common and socially isolating condition characterised by the inadvertent, involuntary loss of stool. Dysfunction of the anal sphincters in particular may lead to loss of defaecatory control and if basic conservative measures fail to provide symptomatic benefit, investigation of anorectal physiological function is warranted.

Anorectal manometry (the study of coordinated mechanical activity of the rectum and anus) is the most commonly performed investigation of anorectal function. Despite this, there appears to be no fixed standard for the technology, protocol or method used for results reporting. Such disparity between institutions is likely to have a significant negative impact on patient management and requires further investigation.

The last decade has seen the introduction of a novel method for manometric data capture and analysis in the form of high-resolution manometry. Application of this technique to the upper GI tract has led to adoption of this technique as the gold standard for assessment of oesophageal manometry however it is yet to be applied extensively to the anorectum. High-resolution anal manometry may have the ability to more accurately appreciate global anorectal function in both clinical and research settings and it is this exploration that is the overall aim of this thesis.

1.6 Specific aims of this thesis

The aims of this thesis are to:

(7) Explore existing practices of anorectal manometry
(8) Examine current evidence for the use of HRAM
(9) Develop and validate a protocol for the performance of HRAM
(10) Define normal values for traditional measures of sphincteric function using HRAM
(11) Develop and validate novel measures of sphincteric function, and explore whether they improve diagnostic accuracy in patients with FI
(12) Examine anorectal function over a prolonged period with HRAM to evaluate the phenomenon of anal sampling in both health and patients with FI

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Chapter 2

2 International survey of methods for anorectal manometry: An exploration of variability in current practice

2.1 Rationale

Due to the appreciation that similar symptoms may result from differing underlying pathophysiologies, assessment of anorectal function is a routine part of symptom investigation in patients with faecal incontinence (FI) (Barnett et al., 1999, Diamant et al., 1999, Scott and Gladman, 2008). Anorectal manometry (ARM) is the most established of these investigations, in part due to the fact that sphincteric dysfunction secondary to obstetric injury is often cited as the leading cause of symptom generation (Rao, 2004, Bharucha et al., 2005, Raizada et al., 2011).

Anorectal manometry typically consists of a series of manoeuvres designed to interrogate involuntary function of the anal canal during rest, voluntary function during squeeze, reflex recto-anal co-ordination during rectal stimulation and voluntary rectoanal co-ordination during push (Scott and Gladman, 2008). Results may be used to direct patient management and are commonly used as a tool for clinical research (Rao and Patel, 1997).

A number of reasonably sized normative datasets for ARM exist within the literature (Cali et al., 1992, Chaliha et al., 2007, Gundling et al., 2010, Noelting et al., 2012, Schuld et al., 2012) however close examination of the methodology demonstrates striking dissimilarities in the equipment used, study protocol and results reported (Cali et al., 1992, Chaliha et al., 2007, Gundling et al., 2010, Schuld et al., 2012, Noelting et al., 2012).

This is despite the appreciation that nuances of study protocol are likely to impact derived results (Schouten and van Vroonhoven, 1983, Rao et al., 1999, Rao et al., 2002, Heinrich et al., 2013) and cause difficulty with results interpretation, transfer of data between institutions, research collaboration and development of expertise. For this reason, several position statements and working party reports have attempted to provide guidance on the optimal technique and reporting (Keighley et al., 1989, Barnett et al., 1999, Azpiroz et al., 2002, Rao et al., 2002). Nevertheless, anecdotal evidence suggests significant variation in local practices (Carrington et al., 2014c).

2.2 Aims

The aim of this study was to examine and compare international practices of anorectal manometry.

2.3 Methods

A questionnaire examining features of anal manometry practice was created using a web-based survey and data collection tool (www.qualitrics.com, Utah, USA). Data were collected in the form of single or compound answer multiple-choice questions for nominal data, slider bar questions for continuous numerical data and open-ended text boxes for descriptive exploration of complex practices.

Questions explored -

1) Department setup
2) Study indications
3) Pre-study assessment
4) Manometry technique and background
5) Catheter specifications
6) Study protocol
7) Additional investigations
8) Data analysis and reporting

The full questionnaire may be reviewed in Appendix A.

Clinicians with an interest in anorectal physiology were identified and contacted by email via advocates from neurogastroenterological societies (the European Neurogastroenterology and Motility Society [ENMS], the Asian Neurogastroenterology and Motility Association [ANMA], the Australasian Neurogastroenterology and Motility Association [ANGMA] and the American Neurogastroenterology and Motility Society [ANMS]), invitation to those attending the 2013 Pelvic Floor Society Annual Meeting, and though industry members and clinicians involved in the International Anorectal Physiology Working Group (IAPWG).

Prior to launch, the questionnaire was piloted to test usability, understanding, clarity and question flow. It included 45 questions and took approximately 20 min to complete. There was no incentive utilised to increase response rate. The survey sent to respondents in the UK between September – October 2013 and internationally between August – October 2014. Responses not completed within 7 days of commencement were discarded.

This work was undertaken with the endorsement of the societies involved. Data were collected and held within the requirements of the Data Protection Act. The study did not use clinical data and did not require or seek ethical approval.

2.4 Results

Sixty-six complete responses were collected from 113 surveys started (54% completion rate). No data pertaining to invitations sent without survey commencement were available. Four responses were received from individuals describing a centre for which a response had already been completed. After discarding duplicate responses 62 complete surveys were available for analysis.
Responses were collected from 12 countries (Figure 2-I). The majority of responses were from European centres (49/62 [79%]) with 29/62 [47%] from the United Kingdom (Table 2-I).

Figure 2-I Annotated world map demonstrating world distribution of responses (N = 62).

Response count -
How many studies are performed in your institution each year?

	Count	Percent	Cumulative Percent
< 50 (less than 1 per week)	3	4.8	4.8
50 - 100 (1 - 2 per week)	8	12.9	17.7
100 - 200 (2 - 4 per week)	17	27.4	45.1
200 - 500 (4 - 10 per week)	18	29	74.1
500 - 1000 (10 - 20 per week)	12	19.4	93.5
> 1000 (more than 20 per week)	4	6.5	100
Total	62	100	

Table 2-I Table of response frequency demonstrating geographical distribution of survey respondents. The majority (79%) of respondents were from centres in Europe.

2.4.1 Department setup

Thirty-four respondents (55%) were from moderate – high volume centres that performed ≥ 4 anorectal manometric studies per week. Three responses were from very low volume centres (2 from Germany an d1 from the United Kingdom) performing < 1 study per week (Table 2-II).

Response count -
How many studies are performed in your institution each year?

	Count	Percent	Cumulative Percent
< 50 (less than 1 per week)	3	4.8	4.8
50 - 100 (1 - 2 per week)	8	12.9	17.7
100 - 200 (2 - 4 per week)	17	27.4	45.1
200 - 500 (4 - 10 per week)	18	29	74.1
500 - 1000 (10 - 20 per week)	12	19.4	93.5
> 1000 (more than 20 per week)	4	6.5	100
Total	62	100	

Table 2-II Table of response frequency demonstrating manometric activity of survey respondents.

Twenty-eight (45%) respondents described their centre as being within a specialist/tertiary hospital, 28 (45%) within a general hospital, 4 (6%) within a private clinic, 1 within an academic research institution and 1 (1.6%) within a rehabilitation unit. Of the 11 respondents from centres performing < 2 studies per week, 4 were from specialist/tertiary hospitals, 6 were from general hospitals and 1 was from a private clinic.

2.4.2 Study indications

Interrogation of the indications for manometric testing demonstrated that all 62 centres either 'sometimes' or 'often' performed studies for constipation and evacuatory difficulties.

One centre (1/62 [2%]) within a specialist hospital in Germany, reported that they 'never' performed manometry for urge faecal incontinence or faecal leakage and this group together with three further centres (total 4/62 [7%]) also reported never performing manometry for faecal urgency.

Fifty-nine (59/62 [95%]) respondents stated either 'sometimes' or 'often' performing anal manometry for the purposes of pre-operative sphincter assessment. Fifty-eight (58/62 [94%]) reported 'sometimes' or 'often' performing anal manometry as part of routine following obstetric injury.

The use of anal manometry for primary investigation of anal pain and abdominal pain were reported less frequently. These data are displayed in the stacked bar chart (Figure 2-II) below.

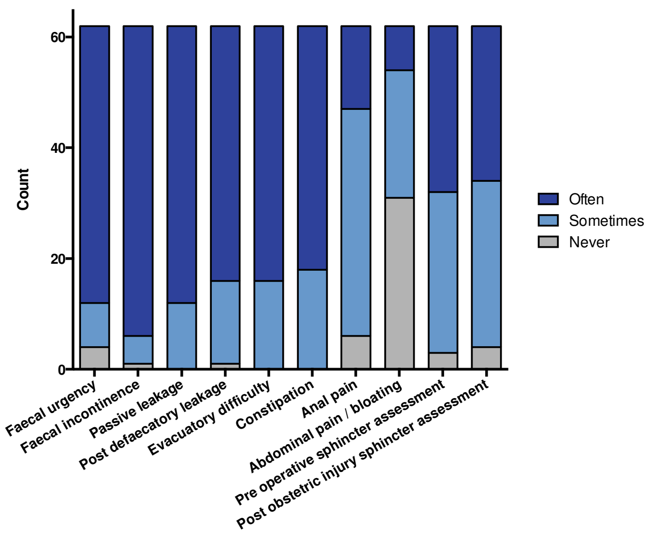


Figure 2-II Stacked bar chart displaying responses to the question 'In your department, how often is anorectal manometry performed for the following indications?' (N = 62).

2.4.3 Pre-study assessment

As part of pre-procedure preparation, 52/62 (58%) centres reported that validated scores were used to assess symptom severity. Of these, 32 centres used a single score, 11 used multiple scoring systems and 9 did not report which scoring system was used.

For the assessment of symptoms of faecal incontinence, scores used in descending order of frequency were: the Wexner score (31/62 [50%]), the St Mark's Faecal Incontinence score (13/62 [21%]), the Pescatori score (1/62 [1.6%]), the American Medical Systems score (1/62 [1.6%]), the Douglas Wong score (1/62 [1.6%]), the Faecal Incontinence Severity Index (1/62 [1.6%]). One centre (1/62 [1.6%]) used an 'in house bothersome score'.

For the assessment of symptoms of constipation, scores used in descending order of frequency were: the Cleveland Clinic constipation score (16/62 [26%]), the Obstructive Defaecation Score (10/62 [16%]), the KESS score (6/62 [10%]), PAC-SYM (6/62 [10%]) and the Constipation Assessment Score (6/62 [10%]).

As a further part of pre-procedure preparation, 36/62 centres reported that either a formal or informal quality of life assessment was performed. The methods used in descending order of frequency were: the SF- 36 (17/62 [27%]), informal / 'in-house' assessment (17/62 [27%]), PAC QoL, (6/62 [10%]), GI QoL (5/62 [8%]) and Rockwood FI QoL (2/62 [3%]).

2.4.4 Complementary investigations of anorectal function

No centre reported performing anal manometry in isolation. All centres reported performing at least 1 further allied study for the assessment of both FI and constipation. These data are shown in Table 2-III and Table 2-IV below.

Response count -
In addition to anal manometry, how often are the following tests performed for the investigation of faecal incontinence?

	Not performed		Sometimes performed		Routinely performed		Missing		Total
	n	%	n	%	n	%	n	%	N
Rectal sensation (balloon distension)	2	3.2	2	3.2	58	93.5	0	0.0	62
Rectal sensation (electrical stimulation)	52	83.9	6	9.7	4	6.5	0	0.0	62
Rectal sensation / compliance (barostat)	45	72.6	10	16.1	7	11.3	0	0.0	62
Anal sensation (electrical stimulation)	53	85.5	5	8.1	4	6.5	0	0.0	62
Pudendal nerve function (terminal motor latencies)	42	67.7	13	21.0	7	11.3	0	0.0	62
Anal endosonography (endoanal ultrasound)	8	12.9	17	27.4	37	59.7	0	0.0	62
Anal electromyography	46	74.2	12	19.4	4	6.5	0	0.0	62
Saline continence test	58	93.5	4	6.5	0	0.0	0	0.0	62
Balloon expulsion	27	43.5	15	24.2	20	32.3	0	0.0	62
Evacuation proctography	27	43.5	29	46.8	6	9.7	0	0.0	62
Colonic transit	28	45.2	30	48.4	4	6.5	0	0.0	62
Colonic scintigraphy	54	87.1	8	12.9	0	0.0	0	0.0	62

Table 2-III Table summarising the use of investigations allied to anal manometry for the investigation of faecal incontinence (N = 62).

Response count -
In addition to anal manometry, how often are the following tests performed for the investigation of constipation?

	Not performed		Sometimes performed		Routinely performed		Missing		Total
	n	%	n	%	n	%	n	%	N
Rectal sensation (balloon distension)	2	3.2	1	1.6	57	91.9	2	3.2	62
Rectal sensation (electrical stimulation)	50	80.6	7	11.3	3	4.8	2	3.2	62
Rectal sensation / compliance (barostat)	43	69.4	10	16.1	7	11.3	2	3.2	62
Anal sensation (electrical stimulation)	51	82.3	4	6.5	5	8.1	2	3.2	62
Pudendal nerve function (terminal motor latencies)	45	72.6	10	16.1	5	8.1	2	3.2	62
Anal endosonography (endoanal ultrasound)	15	24.2	28	45.2	17	27.4	2	3.2	62
Anal electromyography	47	75.8	8	12.9	5	8.1	2	3.2	62
Saline continence test	59	95.2	1	1.6	0	0.0	2	3.2	62
Balloon expulsion	20	32.3	13	21.0	27	43.5	2	3.2	62
Evacuation proctography	19	30.6	20	32.3	21	33.9	2	3.2	62
Colonic transit	12	19.4	21	33.9	27	43.5	2	3.2	62
Colonic scintigraphy	50	80.6	10	16.1	0	0.0	2	3.2	62

Table 2-IV Table summarising the use of investigations allied to anal manometry for the investigation of constipation (N = 62, 2 responses missing).

Sixty-one (61/62 [[98%]) centres stated that they perform complementary assessment of rectal sensation. Sixty (60/62 [97%]) reported either 'sometimes' or 'routinely' performing rectal sensitivity to rectal balloon distension, 10/62 [16%]) reported either 'sometimes' or 'routinely' performing rectal sensitivity to electrical stimulation and 17/62 [27%]) reported either 'sometimes' or 'routinely' performing rectal assessment with a rectal barostat.

For the investigation of patients with faecal incontinence, 37 (37/62 [59%]) respondents reported that examination of sphincter morphology with endoanal ultrasound was performed routinely. A further 17 (28/62 [27%]) reported that endoanal ultrasound was performed intermittently ('sometimes'). The use of endoanal ultrasound was reported less frequently for the assessment of patients with constipation (17/62 [27%] centres answering 'routinely' and (28/62 [45%] answering 'sometimes').

For the investigation of patients with constipation, the majority of respondents (49/60 [82%] submitted responses, 49/62 total cohort [79%]) reported that additional examination of parameters of rectal emptying was regularly performed. Thirty-five (35/60 [58%] submitted responses) centres reported either 'sometimes' or 'routinely' performing balloon expulsion and co-incidentally thirty-five centres (35/60 [58%] submitted responses) also reported either 'sometimes' or 'routinely' performing evacuation proctography.

2.4.5 Manometry technique, systems and background

There was marked variation in the reporting of manometry type performed. The majority of centres (35/62 [57%]) described performing traditional / conventional manometry. Twenty-four centres (24/62 [39%]) reported performing the more novel high resolution or 3D high-resolution manometry (Figure 2-III.) High-resolution (including 3D) manometry was more commonly reported by respondents from specialist hospitals (14/28 [50%]) than general hospitals (6/28 [21%]).

In the United Kingdom, 19 (19/29 [66%]) centres reported performing traditional manometry, 2 (2/29 [7%]) vector-volume manometry, 6 (6/29 [21%]) high-resolution manometry and 2 (2/29 [7%]) 3D high-resolution manometry.

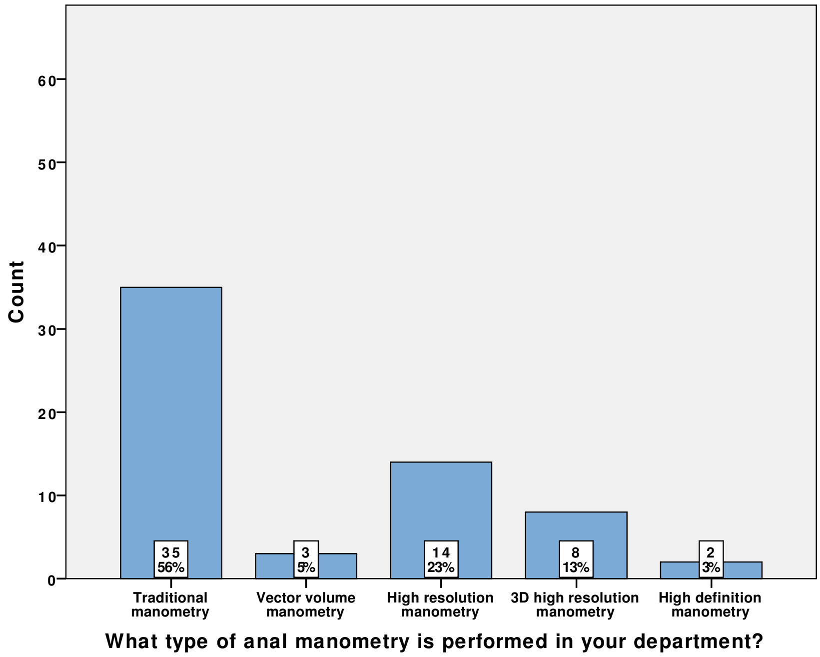


Figure 2-III Bar chart of responses from whole cohort illustrating type of manometry performed (N = 62).

With regards to the catheter type, 35 (35/62 [57%]) centres reported using water-perfused systems and 27 (27/62 [43%]) reported using solid-state systems.

Of the 35 centres that perform traditional manometry, the majority (26/35 [74%]) reported using a water-perfused system. Only 4 of the 14 centres (29%) that perform high-resolution manometry reported using water-perfused technology.

With regards to the units used to report absolute measurements, 18 (18/62 [29%]) centres reported using cmH_20 and 44 (44/62 [71%]) reported using mmHg. Bizarrely, of the 35 centres using a water-perfused system, only 14 (40%) reported absolute measurements in cmH_20 with the other 21 (60%) using mmHg as a unit of measurement. Conversely, 4 of the 27 (15%) centres using centres using solid-state data collection systems reported measurements in cmH_20.

2.4.6 Definition of normal values

Derivation of normal values was variable between centres. Fifteen (15/62 [24%]) centres reported that normal values were derived from a local study of healthy volunteers, 38 (38/62 [61%]) reported utilising data from a published study of normal ranges, 2 (2/62 [3%]) stated that formalised normal range used and 7 (7/62 [11%]) stated that an 'other' method was used.

Of the centres that utilised data from a local study of healthy volunteers 8/15 (53%) admitted that the sample size of this study was less than 40 participants (Figure 2-IV).

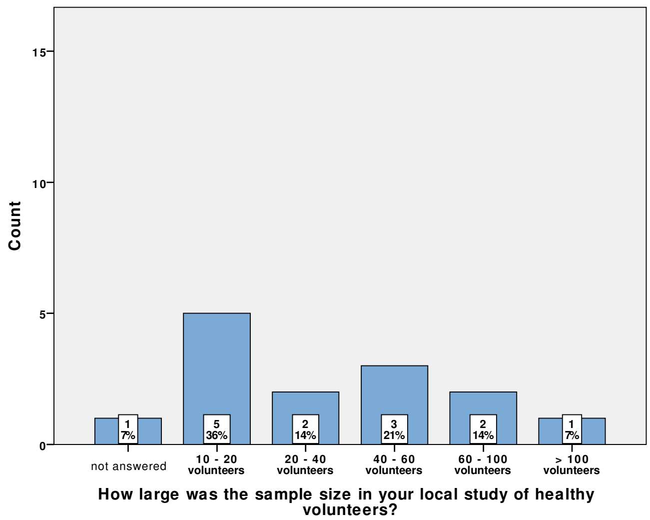


Figure 2-IV Bar chart of responses from centres that utilise a local study of healthy volunteers as the basis for normal values showing sample size of volunteers used (n = 15).

Of the centres that utilised data from published study of normal values, only 14 respondents (14/38 [37%]) could confirm that the equipment set up and study protocol used in their centre was identical to that described within the study (Figure 2-V).

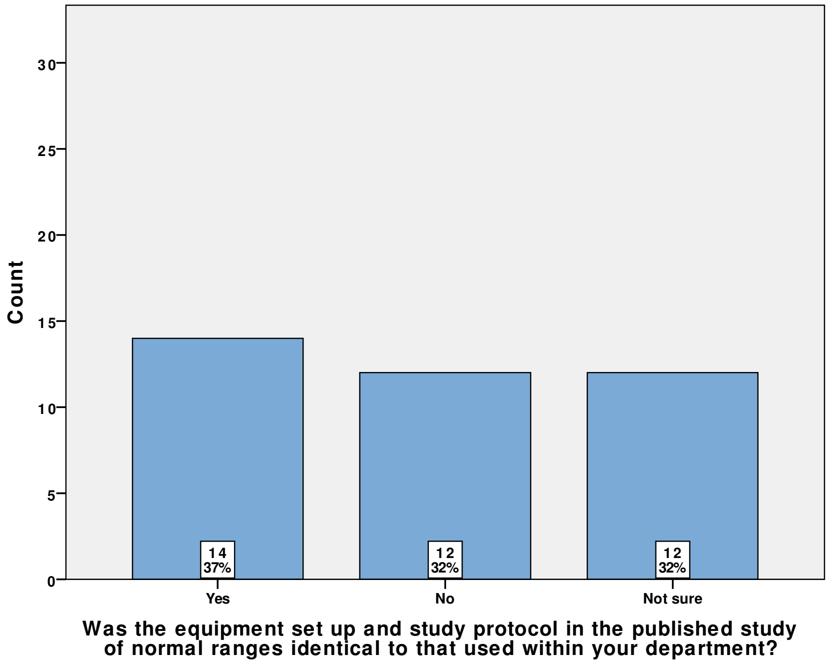


Figure 2-V Bar chart of responses from centres that utilise data from a published study of healthy volunteers as the basis for normal values illustrating reported comparability of local and published equipment and protocol (n = 38).

2.4.7 Catheter configuration

There was marked variation in catheter diameter, sensor number and port configuration between centres. Catheter diameter varied between 8 – 22F for both water-perfused and solid-state systems.

Table 2-V (from centres using water-perfused systems) and Table 2-VI (from centres using solid-state systems) below summarise responses to questions regarding channel / sensor number and port configuration.

a. Response count - How many perfusion channels does your catheter have?

number of channels	Frequency	Percent	Cumulative Percent
2 - 4	6	17.1	17.1
5 - 8	24	68.6	85.7
9 - 12	2	5.7	91.4
>12	2	5.7	97.1
I'm not sure	1	2.9	100
Total	35	100	

b. Response count - How are these channels arranged?

channel arrangement	Frequency	Percent	Cumulative Percent
longitudinally	4	11.4	11.4
spirally	18	51.4	62.9
radially	11	31.4	94.3
longitudinally and radially	2	5.7	100
Total	35	100	

Table 2-V Table summarising responses to questions regarding catheter configuration from respondents that reported using a water-perfused manometry system (n = 35). (a.) Summarises number of perfusion channels, (b.) summarises channel arrangement.

a. Response count - How many sensors does your manometry catheter have?

number of sensors	Frequency	Percent	Cumulative Percent
1	1	3.7	3.7
2 - 4	7	25.9	29.6
5 - 8	3	11.1	40.7
9 - 12	5	18.5	59.3
13 - 20	1	3.7	63.0
21 - 40	2	7.4	70.4
> 40	8	29.6	100
Total	27	100	

b. Response count - How are these sensors arranged?

channel arrangement	Frequency	Percent	Cumulative Percent
longitudinally	8	29.6	29.6
radially	6	22.2	51.9
longitudinally and radially	13	48.1	100.0
Total	27	100	

Table 2-VI Table summarising responses to questions regarding catheter configuration from respondents using a solid-state manometry system (n = 27). (a.) Summarises number of sensors, (b.) summarises channel arrangement.

2.4.8 Manoeuvres performed

Exploration of the manometric manoeuvres utilised for assessment of FI and constipation demonstrated anal resting pressure and anal squeeze pressure were the only tests consistently performed by all centres.

During investigation of FI, 50 (50/62 [81%]) centres reported performing assessment of prolonged anal squeeze, 53 (53/62 [86%]) reported performing assessment of cough, 48 (48/62 [77%]) attempted defaecation and 59 (50/62 [95%]) assessment of the recto-anal inhibitory reflex (RAIR) (Figure 2-VI).

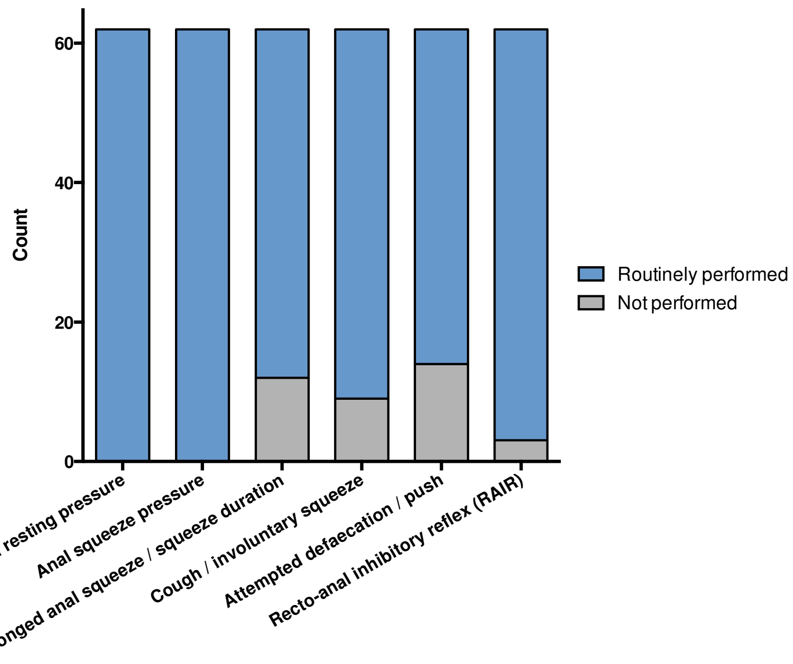


Figure 2-VI Stacked bar chart illustrating variation between centres in manoeuvres performed during manometric assessment of patients with faecal incontinence (N = 62).

During investigation of constipation, 47 (47/62 [76%]) centres reported performing assessment of prolonged anal squeeze, 46 (46/62 [74%]) performing assessment of cough, 51 (51/62 [82%]) attempted defaecation and 60 (60/62 [97%]) assessment of the recto-anal inhibitory reflex (RAIR) (Figure 2-VII).

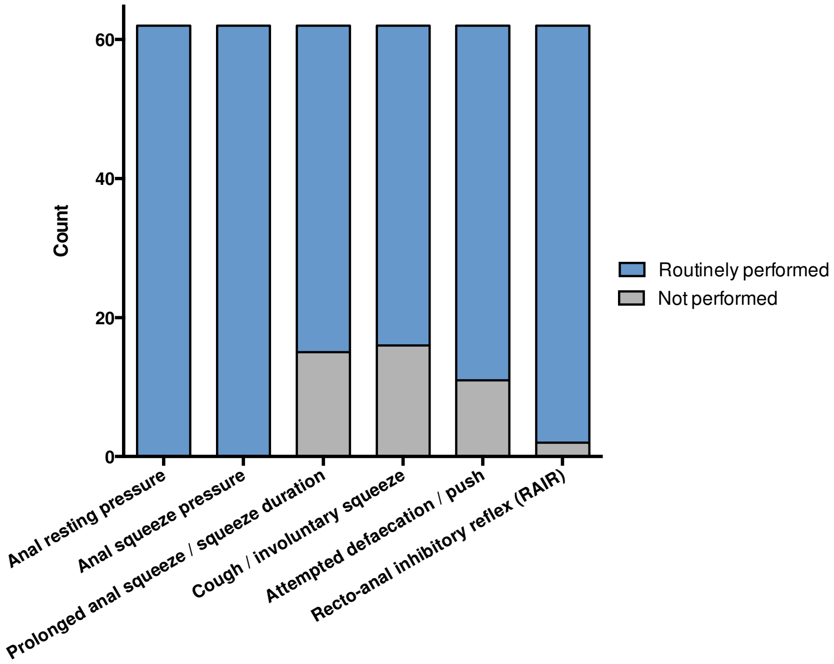


Figure 2-VII Stacked bar chart illustrating variation between centres in manoeuvres performed during manometric assessment of patients with constipation (N = 62).

2.4.9 Anal resting pressure – test performance and reporting

All centres reported performing assessment of anal resting pressure in patients with either FI and / or constipation.

The time given to record anal pressure (minutes) was reported to be variable between centres. Nine centres (9/62 [15%]) reported measurement of anal pressures over < 1 minute, 40 centres (40/62 [65%]) reported measurement over between 1 – 2 minutes and 12 (12/62 [19%]) reported measurement over between 3 – 5 minutes.

There was particular variation in the methods used to report results. The most commonly reported parameter to describe rest was 'mean pressure over the whole anal canal' (reported by 47%). These data are further summarised in Table 2-VII below.

Reponse count -
Which parameters are used to report anal resting pressure?

	Not reported		Reported		Total
	n	%	n	%	N
Mean pressure at different levels of the anal canal	38	61	24	39	62
Mean pressure over the whole anal canal	33	53	29	47	62
Maximum pressure at different levels of the anal canal	50	80.6	12	19	62
Maximum pressure over the whole anal canal	42	67.7	20	32	62
Other	56	90.3	6	10	62

Table 2-VII Table summarising responses to the multiple answer question regarding results reporting for measures of anal resting pressure (N = 62).

In those 13 centres that perform radial analysis of pressure (vector volume manometry, 3D HRAM or high definition HRAM), 5 institutions reported either 'sometimes' or 'always' quantifying anal symmetry.

As questions were designed as 'select all that apply', it was possible to assess the combination of measurement parameters utilised by each institution. This analysis demonstrated that there were 16 combinations of ways in which rest data were quantitatively reported. The three most common reporting methods were 'mean pressure over the whole anal canal length' alone (24%), 'mean pressure at different levels of the anal canal' alone (22%), and 'maximum pressure over the whole anal canal' alone (14%).

2.4.10 Anal squeeze pressure – test performance and reporting

All centres reported performing assessment of anal squeeze pressure in both patients with both FI and constipation.

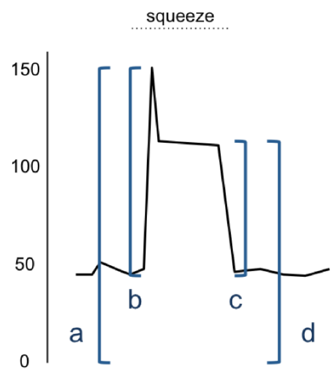
Thirty-nine (39/62 [63%]) respondents stated that during assessment of anal squeeze pressure, patients are asked to squeeze for a predefined length of time, the other 23 (23/62 [37%]) respondents stated that patients are asked to squeeze for as long as they were able.

Of those that asked patients to squeeze for a predefined length of time, 4 (4/62 [6%]) centres reported that a 30-second squeeze is performed, 6 centres (6/62 [10%]) reported that a 20-second squeeze is performed, 2 (2/62 [3%]) a 15-second squeeze, 14 (14/62 [23%]) a 10-second squeeze and 13 (13/62 [21%]) a 5-second squeeze.

There was also discrepancy between centres in the number of squeeze performed during manometry. Two respondents (2/62 [3%]) reported that patients are asked to perform a single squeeze, 50 centres (50/62 [81%]) reported that 2 – 3 squeezes are performed and 10 centres (10/62 [16%]) reported that > 3 squeezes are performed.

As with parameters of resting anal pressure, there was marked variation in the methods used to report results. The two most common squeeze parameters reported were 'maximum incremental squeeze pressure' (63%) and 'maximum absolute squeeze pressure' (50%). These data are further explored in Table 2-VIII below.

Similar to rest, there were 16 combinations of ways in which squeeze data were quantitatively reported. The two most common reporting methods were 'maximum incremental squeeze pressure' alone (24%), 'maximum absolute squeeze pressure' with 'maximum absolute squeeze pressure' (13%).



Reponse count -
Which parameters are used to report anal squeeze pressure?

	Not reported n	Not reported %	Reported n	Reported %	Total N
a (maximum absolute squeeze pressure)	31	50	31	50	62
b (maximum incremental squeeze pressure)	23	37	39	63	62
c (sustained incremental squeeze pressure)	36	58.1	26	42	62
d (sustained absolute squeeze pressure)	48	77.4	14	23	62
other	60	96.8	2	3	62

Table 2-VIII Figure and table summarising responses to the multiple answer question regarding results reporting for measures of anal squeeze pressure (N = 62).

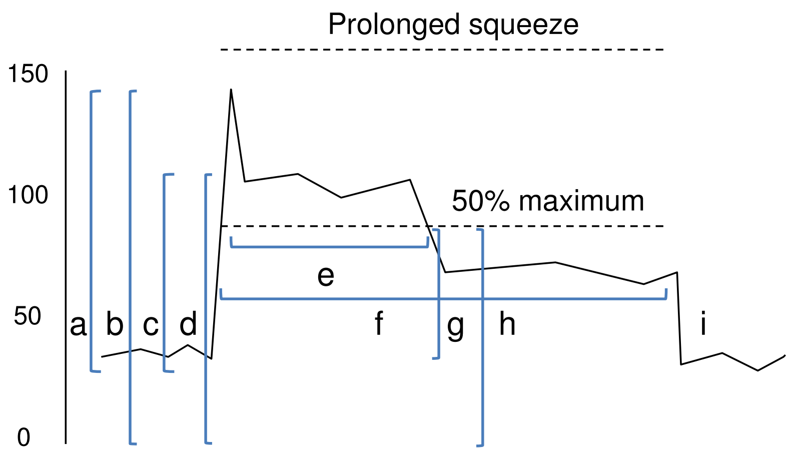
In those that performed high-resolution manometry, further exploration with a multiple answer question revealed that 19 respondents (19/24 [79%]) described reporting quantitative results from the in-built analysis software, 7 (7/24 [29%]) described reporting quantitative results derived manually from line traces and 7 (7/24 [29%]) described qualitative results reporting from inspection of the colour contour images.

In those with vector volume or 3D high-resolution manometry 5 (38%) respondents described reporting squeeze symmetry either 'sometimes' or 'routinely'. Of these, further evaluation with a multiple answer question revealed that 3 respondents reported this quantitatively and 4 reported symmetry qualitatively.

2.4.11 Prolonged squeeze – test performance and reporting

Similar to the results found with anal squeeze pressure, there was marked variation in the performance and reporting of the prolonged squeeze manoeuvre. Nineteen (19/50 [38%]) centres reported performing prolonged squeezes over 30-60 seconds and 31 (31/50 [62%]) centres reported performing prolonged squeezes over 5 – 25 seconds.

There was particular variation in results reporting of this manoeuvre as there were 30 combinations of ways in which prolonged squeeze data were quantitatively reported. The two most common reporting methods were 'duration of squeeze above 50% maximum pressure' alone (14%) and 'duration of squeeze above resting pressure' alone (10%). These data are summarised in Table 2-IX below.



Reponse count -
Which parameters are used to report prolonged squeeze?

	Not reported		Reported		Total
	n	%	n	%	N
a (maximum incremental pressure)	33	66	17	34	50
b (maximum absolute pressure)	35	70	15	30	50
c (incremental sustained pressure)	31	62.0	19	38	50
d (incremental absolute pressure)	36	72.0	14	28	50
e (duration of squeeze above 50% maximum pressure)	30	60.0	20	40	50
f (duration of squeeze above resting pressure)	33	66.0	17	34	50
g (incremental pressure at 50% maximum)	43	86.0	7	14	50
h (absolute pressure at 50% maximum)	45	90.0	5	10	50
Other	42	84.0	8	16	50

Table 2-IX Figure and table summarising responses to the multiple answer question regarding results reporting for measures of prolonged squeeze (N=50).

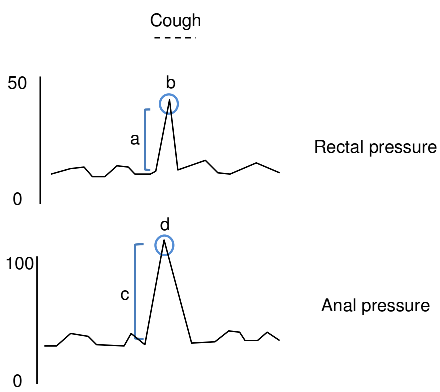
2.4.12 Cough – test performance and reporting

As previously, there was marked variation in the performance and reporting of the cough manoeuvre. With regards to protocol, 3 centres (3/54 [56%]) report asking the subject to cough between 4 – 10 times, 11 (11/54 [20%]) ask the subject to cough 3 times, 21 (21/54 [39%]) ask the subject to cough twice and 18 (18/54 [33%]) ask the subject to cough once.

With regards to reporting, 34 (34/54 [63%]) described reporting the cough quantitatively and 21 (21/54 [39%]) report the cough qualitatively only.

Of those that report cough measures quantitatively, 33 (33/54 [61%]) respondents described reporting both rectal and anal pressures, 16 (16/54 [31%]) described reporting anal pressures only and 5 (5/54 [9%]) reported that neither rectal nor anal pressures are measured.

There were 11 combinations of ways in which cough data were quantitatively reported. The two most common combinations were the use of 'maximum anal pressure' alone (17%) and 'change in rectal pressure during cough' together with 'change in anal pressure during cough' (7%). Measures used for reporting of cough results are summarised in Table 2-X below.



Reponse count - Which parameters are used to report cough?

	Not reported		Reported		Total
	n	%	n	%	N
a (change in rectal pressure during cough)	44	81	10	19	54
b (maximum rectal pressure during cough)	46	85	8	15	54
c (change in anal pressure during cough)	37	68.5	17	31	54
d (maximum anal pressure during cough)	36	66.7	18	33	54
c - a (subtract pressure a from pressure c) = anorectal pressure difference during cough	45	83.3	9	17	54
Other	54	100	0	0	54
Quantitative values are not reported	34	62	21	38	55

Table 2-X Figure and table summarising responses to the multiple answer question regarding results reporting for measures of cough (N=54).

In those with the ability to measure radial pressures (25%) respondents described reporting cough symmetry either 'sometimes' or 'routinely'. Of these, further evaluation with a multiple answer question revealed that 1 respondent reported this quantitatively and both reported symmetry qualitatively.

2.4.13 Attempted defaecation / push – test performance and reporting

Fifty-one centres (51/62 [82%]) reported performing assessment of the push manoeuvre. As with other manoeuvres there were noticeable dissimilarities in test performance and results reporting between centres.

When questioned about subject positioning, 41 (46/51 [80%]) centres reported that the test is performed with the subject in the left lateral position, 2 (2/51 [4%]) with the subject sitting on a commode, 3 (3/51 [59%]) with the subject supine, 1 (1/51 [2%]) with the subject in another unspecified position and 4 (4/51 [8%]) with the subject in both the left lateral and sitting position (Figure 2-VIII).

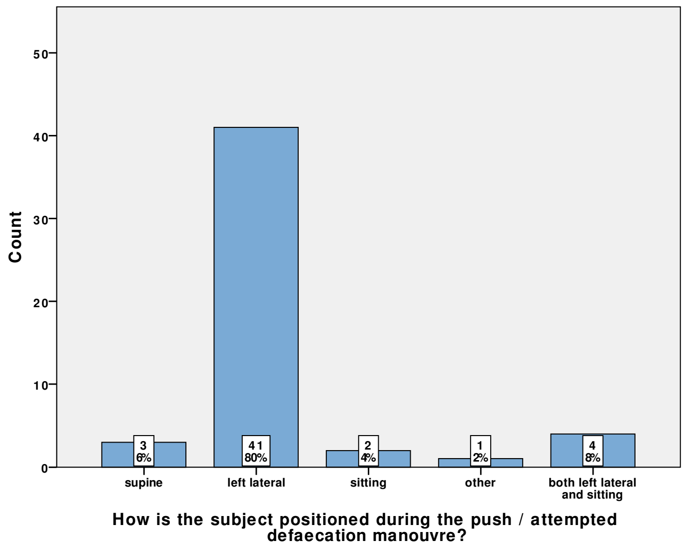


Figure 2-VIII Bar chart of responses pertaining to subject positioning during the push manoeuvre (N = 51).

Thirty-seven (37/51 [73%]) respondents reported that during the manoeuvre a balloon is placed in the rectum. Of these, 7 centres (7/37 [19%]) fill the balloon to the subjects' first sensory volume, 7 (7/37 [19%]) to the subjects' defaecatory desire volume and 21 (21/37 [57%]) to a pre-defined fixed amount. This mean pre-defined volume was 41mls and volumes ranging from between 10 – 60mls were reported.

Only 36 centres (36/51 [71%]) reported the measurement of both rectal and anal pressures during the cough manoeuvre. Six centres (6/51 [12%]) measured neither rectal nor anal pressures (Figure 2-IX.).

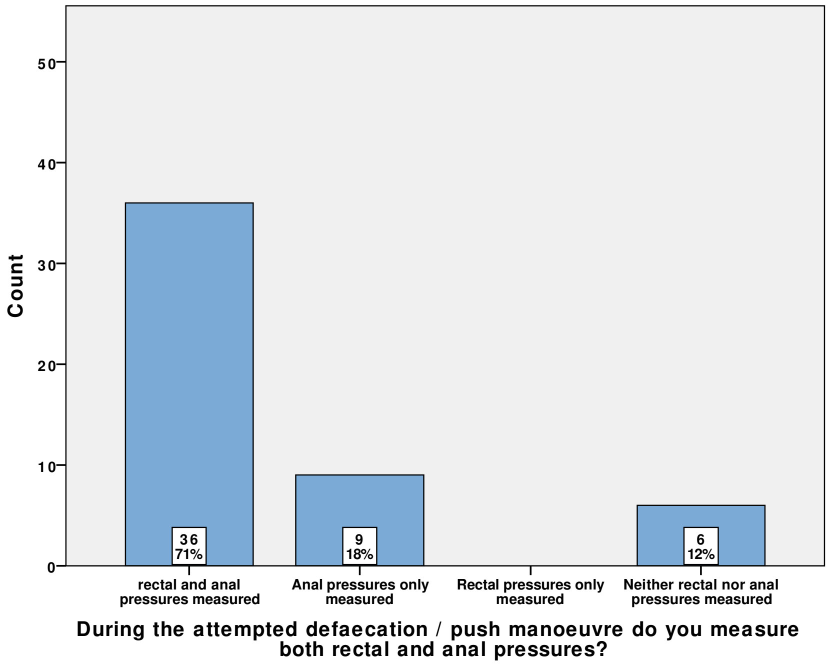
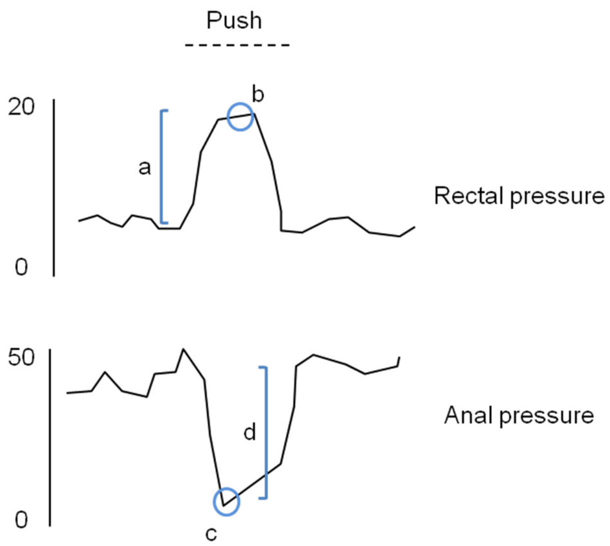


Figure 2-IX Bar chart of responses pertaining to pressure measurement during the push manoeuvre (N = 51).

In a multiple answer setting, 14 centres (14/51 [27%]) stated that results for the push manoeuvre were reported quantitatively using in-built analysis software, 19 (19/51 [37%]) that results are reported quantitatively deriving values manually from line traces, 7 (7/51 [14%]) described results reporting as qualitative from colour contour / line traces and 19 (19/51 [37%]) stated that the numeric results of the push test are not reported i.e. only visualisation of appropriate muscle recruitment / co-ordination is reported.

In centres that reported quantitative analysis of push data, there were 17 combinations of ways in which push data were reported. The 2 most common combinations were 'rectal pressure during push' with 'change in anal pressure during push' (10%) and 'change in anal pressure during push' alone (10%). Response frequencies for methods used to report of attempted are summarised in Table 2-XI below.



Reponse count -
Which parameters are used to report push / attempted defaecation?

	Not reported		Reported		Missing		Total
	n	%	n	%	n	%	N
a (change in rectal pressure during push)	37	77	11	23	3	6.3	48
b (rectal pressure during push)	31	65	17	35	3	6.3	48
c (minimum anal pressure during push)	35	72.9	13	27	3	6.3	48
d (change in anal pressure during push)	28	58.3	20	42	3	6.3	48
Push percentage (percentage fall in anal pressure from baseline)	39	81.3	9	19	3	6.3	48
Rectoanal gradient	43	89.6	5	10	3	6.3	48
Other	45	93.8	3	6	3	6.3	48
Quantitative values are not reported	34	70.8	14	29	3	6.3	48

Table 2-XI Figure and table summarising responses to the multiple answer question regarding results reporting for measures of push / attempted defaecation (N = 48).

2.4.14 Rectoanal inhibitory reflex (RAIR) – test performance and reporting

Sixty-one centres (61/62 [98%]) reported that study of the RAIR was a routine part of anorectal manometry.

Fifty respondents (50/62 [81%]) reported that the RAIR is provoked by incremental inflation of the rectal balloon with fixed volumes of air until a RAIR is seen and 11 (11/62 [18%]) reported that the RAIR is provoked by inflation of the rectal balloon with a single fixed volume of air.

In those 11 respondents that report using a single fixed volume of air, the volume used ranged from 20 – 80mls (mean 55mls). In those 50 respondents that report incremental inflation of the rectal balloon, there was more variation in initial balloon volumes (Figure 2-X).

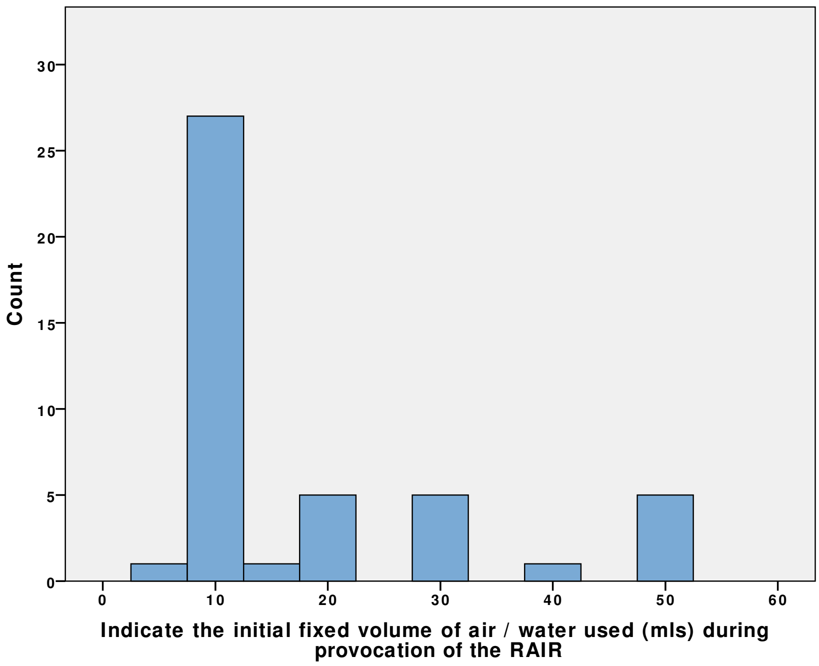


Figure 2-X Histogram illustrating initial fixed volume of air used during provocation of the RAIR reported by centres that perform studies using an incremental inflation technique (N = 50).

In a multiple answer setting, reporting of the RAIR was described as quantitative (volume required to elicit response) by 44 (44/61 [72%]) respondents and qualitative (present / absent) by 42 (42/61 [69%]) respondents. Twenty-five (25/61 [41%]) respondents reported that data are presented quantitatively and qualitatively (Figure 2-XI).

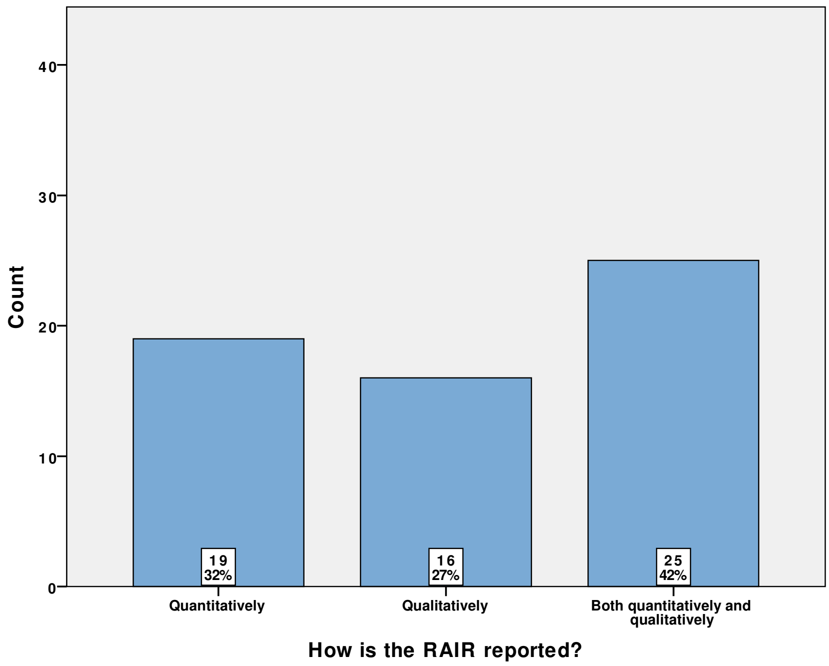


Figure 2-XI Bar chart illustrating method of reporting described for the rectoanal inhibitory reflex (N=61).

2.4.15 Compliance with current accepted guidelines

A comparison was made between responses and the manuscript commonly accepted as the 'minimum standards of anorectal manometry' (Rao et al., 2002). This manuscript recommends a minimum 6-sensor catheter with performance of the rest, squeeze, cough, push and RAIR manoeuvres. It advises reporting of the following basic parameters: maximum anal resting pressure at intervals within the anal canal, maximum anal incremental squeeze pressure, squeeze duration, rectoanal pressure difference during cough, residual anal pressure during push and combined qualitative/quantitative reporting of the RAIR. Only one centre (within a tertiary Hospital in Zürich, Switzerland) was found that fulfilled these minimum standards. A further comparison between centres demonstrated that no two centres reported identical manometric protocols.

2.5 Discussion

This study confirms the long held impression that striking variation exists in the current practice of anorectal manometry. Differences between institutions exist in study indications, equipment used, manometry technique, data acquisition, analysis and reporting. Only one centre responding to this survey fully complies with previously published and widely cited 'minimum standards' for anorectal manometry (Rao et al., 2002). In particular, there is dissimilarity in the parameters used to report results, a factor that makes accurate comparisons between institutions and further development of the technique challenging.

In an environment in which several commercial entities are developing and manufacturing diagnostic technologies, a degree of variation is inevitable and may be welcomed for the purposes of innovation. However, when such techniques are applied to clinical practice, nuance in equipment characteristics can have important effects on manometry measurements. This has been studied in both the upper and lower GI tract, and although most studies report good correlation between techniques, absolute values do significantly differ (Fang et al., 2004, Simpson et al., 2006, Jones et al., 2007, Vitton et al., 2013c, Kang et al., 2015). This represents a challenge to standardisation, as until robust evidence on actual differences in measurement and analysis exists, practitioners will continue to be driven by personal/institutional preference when choosing device and equipment specifications.

It is clear that the introduction of HRAM has brought with it further variability (Lee and Bharucha, 2016). This survey demonstrates that although conventional manometry is most commonly used in combination with water-perfused technology (74% of institutions surveyed), many of those with more novel

HRAM systems have chosen to use solid-state hardware (71% institutions surveyed). The impact of these differences in hardware/software combinations is yet to be quantified in the anorectum, however studies in the oesophagus indicate that the choice of technology and can impact diagnostic decision-making (Roman et al., 2006, Zerbib et al., 2013, Fox et al., 2015, Carlson et al., 2015).

Differences in practice were not limited to hardware/software combinations, but appeared to pervade all aspects regarding performance of the technique. The impact of variation in study protocol on manometric results and management of patients with anorectal disorders has not been robustly tested however, it has been shown that changes in patient position, doctor-patient interaction and data analysis all have important effects on anorectal measurements that can impact on clinical diagnosis (Thekkinkattil et al., 2007, Heinrich et al., 2013, Ratuapli et al., 2013a).

A number of features found during investigation of study protocol invite discussion. Of particular interest was the finding that the majority of centres perform push in the left lateral position. Although sitting is clearly more physiological, only 12% of centres chose to investigate patients in this manner. It is often argued that testing in the left-lateral position is one reason for the high rate of dyssynergia in both healthy and patient populations (Ratuapli et al., 2013b, Grossi et al., 2016) and investigation in the upright-seated position has been shown to influence rectal and anal pressure (Heinrich et al., 2016, Rao et al., 2006). Certainly further exploration of the impact of patient position is warranted.

Another area for consideration is the near universal (95% of institutions surveyed) assessment of the RAIR. Although this is viewed as a useful screening test in paediatric populations (to exclude the presence of Hirschsprung disease) no formal evidence of the application of this test in adult populations exist (Emir et al., 1999, De Lorijn et al., 2005), especially as new diagnosis of this disorder in adults is exceptionally rare and usually made on clinical, radiological and histological grounds.

Additionally, despite a lack of evidence for its diagnostic utility (Azpiroz et al., 2002, Rao et al., 2002, Pehl et al., 2007), cough was performed by 86% of centres. The majority reported qualitative values and when quantitative values were reported there was significant variation in results reporting. The significant variation in results reporting between centres surveyed seem to indicate that the rationale for this test is poorly understood.

The finding of discordance in results reporting is particularly interesting. Although current guidelines recommend the utilisation of certain measures for resting and squeeze pressure (Azpiroz et al., 2002, Rao et al., 2002, Pehl et al., 2007) the diagnostic value of the different measures for discriminating health and disease states is limited (Prott et al., 2005, Pehl et al., 2007). This is likely in part to explain the finding that there were 16 combinations of ways in which rest, 16 combinations of ways in which squeeze and 30 combinations of ways in which prolonged squeeze data were quantitatively reported. This inconsistent use of terminology and methods for data acquisition and analysis of ARM findings requires specific discussion because at the very least, such practice can cause confusion when communicating results between practitioners both in the clinical setting and also when published in the literature.

This variability can be partly explained by the fact that there are few published studies that investigate the *comparative* utility of individual manometric measures. There is no evidence to date that demonstrates that one manometric measure conveys superior diagnostic information to another. In addition, although it is well accepted that sphincter pressures are lower in patients with faecal incontinence than in health (Hiltunen, 1985, McHugh and Diamant, 1987, Bielefeldt et al., 1990, Felt-Bersma et al., 1990, Rasmussen et al., 1992, Holmberg et al., 1995, Fernandez-Fraga et al., 2002, Bharucha et al., 2005, Deutekom et al., 2007, Pehl et al., 2012) there is only limited evidence that the *degree* of functional abnormality of the sphincter is related to symptom severity or predictive of treatment success (Hill et al., 1994, Engel et al., 1995, Bharucha et al., 2005, Bordeianou et al., 2008, Wickramasinghe et al., 2015).

It is pertinent to appreciate that current guidelines recognise that patients with symptoms of faecal incontinence and/or constipation typically present with *multiple* abnormalities of structure/function (Bharucha and Rao, 2014, Wald et al., 2014a). For this reason, ARM alone is generally inadequate to establish the true final pathophysiological cause for guiding best treatment. This is reflected in the results of this survey, which demonstrates that the majority of centres utilise allied tests such as colonic transit, balloon expulsion, and rectal sensory testing to balloon distension. None of centers surveyed reported performing ARM in isolation. In this context, it is important to note that the respondents to this survey were centres performing physiology at clinicians' request and it is likely that elements of further testing are performed by other departments e.g. radiology / ultrasound. This is highlighted by the apparently infrequent routine use of endoanal ultrasound (60% of patients presenting for investigation of faecal incontinence) even though this is recognised as the cornerstone of investigation for patients in this context (Sultan et al., 1993a, Sultan et al., 1993b, Kamm, 1994). However, the additional diagnostic utility of adjunctive testing methods is currently not quantified. Indeed, a recent study comparing alternate methods of assessing evacuatory function demonstrated marked disagreement between the results of testing modalities (Palit et al., 2016). This highlights the need for further collaborative efforts to establish gold standards to allow standardized of investigative pathways in these patient groups.

For this reason published guidelines have been generally based on expert experience and opinion rather than an objective comparison of the utility of different measures and allied tests (Scott and Gladman, 2008). Indeed, this lack of consensus may be the reason for the relatively slow adoption and rate of publication with HR-ARM compared to oesophageal HRM for which a well-established method and classification system exists (Kahrilas et al., 2015).

2.5.1 Limitations

The author acknowledges a number of limitations within this study. The first is the method for identification of potential respondents. Efforts were made to identify as many centres as possible through interaction with the neurogastroenterological societies, however the majority of invitations were sent personally via contacts of the IAPWG, which resulted in a convenience sample. This may have lead to significant undercoverage bias as some centres (particularly low volume centres which do not engage formally with the societies) may have been underrepresented in the sample.

In addition it is likely that this survey suffered from significant nonresponse bias. No data pertaining to response rate were collected. Despite interaction with the American Neurogastroenterology and Motility Society and invitations sent to a number of centres within the US, only one centre from North America submitted a complete response. It is possible that these non-respondents differed in meaningful ways from those who completed the survey resulting in voluntary response bias.

Furthermore, due to the complexity of results recording, options for reporting of certain manometric measures and measures of centre activity had to be given as close ended, leading questions. This may have lead to response bias due to the lack of study blinding and resultant social desirability. In particular, as the survey was created by a centre that does not routinely perform radial analysis of manometric data, there was a lack of specific closed questions relating to vector volume, 3D measurements and specific features of complex anorectal events such as the RAIR. This may explain the relatively low (38%) reported rate of measuring symmetry in those centres with the capability to do so.

Finally, due to the efforts of key individuals in the United Kingdom over 40% of responses were collected from British centres. Therefore, although responses have been collected from centres around the world, it is unlikely that results are a true reflection of global practices and more likely that there is a strong bias to practices within the UK and Europe.

2.5.2 Implications of this study

This study provides the first formal evidence of discordance in international practices of anal manometry. It has demonstrated that methods of both data collection and results reporting are extremely variable and it is likely that many centres are not following currently acknowledged 'best practice'. This disparity is likely to be limiting the utility of this technique, preventing data comparison between institutions and may be impacting on clinical decision-making.

This study provides a basis for the development of agreement and consensus generation regarding the optimal methods of study performance. Further study of best practice and promotion of the need for standardisation of protocol will likely reduce unacceptable and undesirable variations in practice.

Ultimately, the formation of good clinical guidelines for anorectal manometry is likely to have a significant impact on both the clinical and research applications of this technique.

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Chapter 3

3 Review of high resolution anorectal manometry and its current place in clinical work and in research

3.1 Introduction

The objective assessment of anal sphincter function with anorectal manometry is routine practice in patients presenting to a tertiary centre with symptoms of disordered defaecation (Rao et al., 2002, Scott and Gladman, 2008).

Though protocols vary, this assessment of anorectal pressures has until recently, been performed through utilization of manometric catheters that incorporate a limited number of sensors (≤ 6) with data from each recording point interpreted separately (Rao, 1996, Rao, 1997, Sun and Rao, 2001, Rao et al., 2002, Scott and Gladman, 2008). This practice is typically termed conventional anal manometry (CAM).

Recent technological advancements have enabled the development of manometric systems with the ability not only to collect data from an increased number of sensors, but also to display and analyze data in a format that allows a more global appreciation of structure and function. Clouse and Staniano first introduced this 'high resolution' method of acquisition and analysis in the early 1990's for the investigation of the upper gastrointestinal tract. Data pertaining to sensor position, average pressure and time were transformed into pseudo-3D topographic plots to better illustrate functional anatomy (Clouse and Staiano, 1991, Clouse and Staiano, 1993).

Since this time, high-resolution manometry has been demonstrated to significantly improve yield and diagnostic accuracy of oesophageal dysfunction when compared to conventional manometry (Fox et al., 2004, Fox and Bredenoord, 2008) and is now the gold-standard method for data acquisition and analysis (Bredenoord et al., 2012).

The same is true for manometry applied to the colonic tract. A recently published paper exploring the influence of sensor spacing on ability to identify colonic propagating sequences demonstrated that tripling of the sensor spacing from 1 to 3 cm resulted in a 30% chance of misinterpretation of recorded activity (Dinning et al., 2013).

Application of high-resolution manometry to the anorectum is more recent with the first study detailing its use published in 2007 (Jones et al., 2007). A recent increase in interest has provoked the production of a number of high-resolution systems available for use in both clinical and research settings. These include 2-dimensional systems, which utilise data from a catheter that typically houses between 8 – 12 longitudinal sensors (Carrington et al., 2014a), and 3-dimensional systems, which collect and individually report data from sensors placed not only longitudinally but also radially (Cheeney et al., 2012).

Although data are emerging utilizing high-resolution anorectal manometry (HRAM), there is currently no consensus as to the additional utility of this technique over CAM.

3.2 Aims

The aim of this study was to collate and examine all published literature pertaining to HRAM.

3.3 Methods

A review of the literature was performed in February 2015. This aimed to identify clinical papers describing the utility of HRAM / 3D HDAM.

The search was performed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) framework (Liberati et al., 2009). Manuscripts of interest were found by interrogation of the PubMed, EMBASE, OVID and Medline databases. The search terms 'high resolution anal manometry', 'high-resolution anorectal manometry', 'high definition anal manometry', '3D anal manometry', 'three-dimensional anal manometry' and 'anorectal manometry' were used.

Full-text manuscripts of articles written in English were reviewed for relevance. All studies reporting physiological data obtained with high-resolution anal manometry were included. High-resolution manometry was defined as investigations performed with a manometric catheter incorporating sensors places ≤8mm apart and with data displayed in colour-contour format.

Due to the small number of published articles on the topic, for reasons of feasibility no exclusion was made on the basis of study design or sample size and there was no blinding of the investigator to author name, institution or manuscript title. Manuscripts were discarded on the basis of the following defined criteria:

1) Article not describing anal manometry
2) Editorial/review article
3) Conventional manometry described
4) Article not in English
5) No relevant data described
6) Study published in abstract form only
7) Case reports

Reference lists of included papers were subsequently hand searched to find further articles of interest, all of which were reviewed in full.

The clinical literature search revealed 76 articles, of which 27 were deemed suitable for inclusion (Figure 3-I).

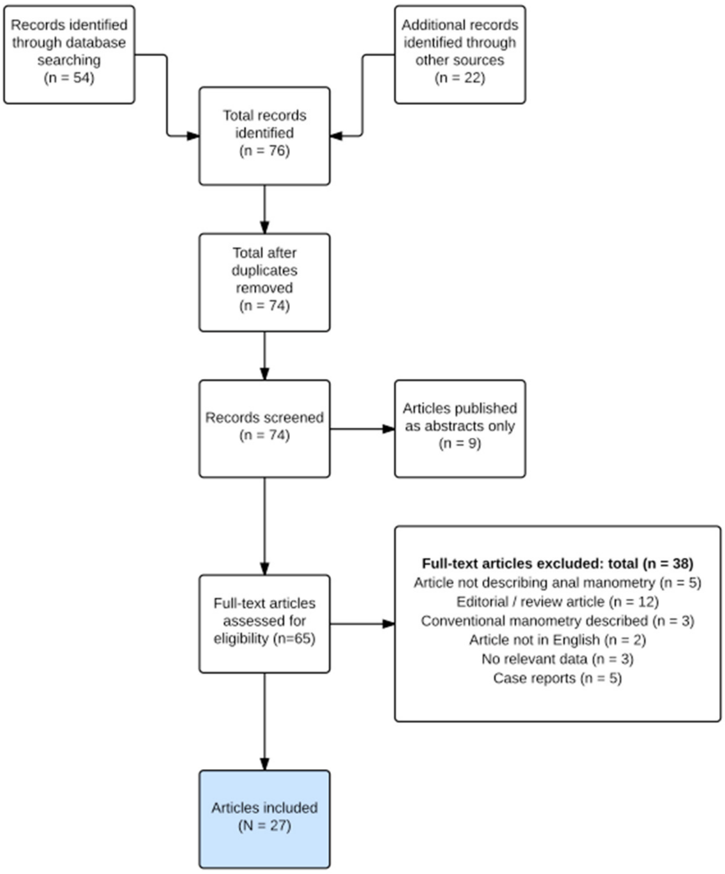

Figure 3-I PRISMA flow diagram illustrating the process followed during identification of included manuscripts.

3.4 Results

Of the 27 studies published, 24 are in adults and 3 are in pediatric populations. Seventeen studies are in various patient groups (constipation: n = 8; constipation or fecal incontinence: n = 5; anal fissure, perineal descent, rectal cancer and

Hirschsprung disease: all n = 1), of which only 4 are controlled the by inclusion of healthy volunteers. The remaining 10 studies have been performed in healthy control subjects. Disappointingly, the majority of studies are of low quality, comprising exploratory case series without sample size analyses, many of which describe data collected retrospectively, which therefore have likely suffered from selection and performance bias.

3.4.1 High-resolution anorectal manometry catheters

Two separate technologies currently exist: high-resolution anorectal manometry (HRAM) (Carrington et al., 2014a), and 3D high-definition anorectal pressure manometry/topography (3D HRAM / HDAM) (Cheeney et al., 2011, Raizada et al., 2011)

High-resolution anorectal manometry systems utilise flexible catheters that typically house 8 – 12 longitudinal sensors spaced approximately 0.6 – 1 cm apart. The most proximal 1 or 2 sensors (often spaced further apart) may be used to record intra-balloon pressure within a balloon attached to the uppermost part of the catheter for rectal distension/sensory testing. The most distal sensor, left outside of the anal canal, records atmospheric pressure. Of the most widely used catheter assemblies, ManoScanTM catheters (Given Imaging, Yoqneam, Israel) contain sensors receiving input from 12 to 36 circumferential elements (Ratuapli et al., 2012) whereas Unisensor catheters (e.g., UniTip, Attikon, Switzerland) measure circumferential pressure either by means of a single pressure sensor embedded within a soft membrane containing silicone gel (Carrington et al., 2014a), or by having 4 radially arranged sensors at each level, from which pressures can be averaged to provide a mean pressure (Jung et al., 2014). Water-perfused HRAM catheters with similar recording site configurations are also available (e.g., Mui Scientific", Mississauga, ON, Canada) (Opazo et al., 2013).

For all catheter-types, proprietary software within dedicated manometry systems are available to amplify, interpolate, display (as either traditional line plots, or contemporary color-contour topographical plots), and analyze recorded pressure signals (e.g., Solar GI system with MMS database software: Medical Measurement Systems B.V., Enschede, The Netherlands; Mano- ViewTM software: Given Imaging; InSIGHT system with Bioview analysis software; Sandhill Scientific, Milwaukee, WI, USA).

The 3D HRAM / HDAM system utilizes a rigid probe (100 mm length, 10.75 mm diameter: Given Imaging) housing 256 pressures sensors. The 'active' area of measurement is 6.4 cm, and hence this technology is better suited for appreciation of anal morphology, rather than interplay between functions of the rectum and anus.

To date, the majority of published studies have utilized either the HRAM ManoScanTM catheter, or the 3D HDAM catheter (roughly equal split). Only a handful of studies thus far have used other technologies. The agreement between recordings acquired using different systems is unclear. Indeed, no study performed in the anorectum has directly compared results obtained from different HRAM/3D HDAM catheters.

3.4.2 Normative data

Only 7 studies published so far, utilizing both HRAM (Noelting et al., 2012, Carrington et al., 2014a, Sauter et al., 2014) and 3D HRAM / HDAM (Li et al., 2013, Lee et al., 2014, Xu et al., 2014, Coss-Adame et al., 2015) technologies, have reported normative ranges in adults for traditional measures of anal sphincter function, including: anal resting pressure, incremental anal squeeze pressure, rectoanal gradient during the push maneuver, and also percentage anal relaxation during push. These values are summarized in Table 3-I.

Author	Year	N M	N F	Article type	2D/3D HRAM	anal resting pressure (mmHg) males	anal resting pressure (mmHg) females	anal squeeze pressures (mmHg) male	anal squeeze pressures (mmHg) females	rectoanal gradient males	rectoanal gradient females	% anal relaxation males	% anal relaxation females
Noelting	2012		30[e] 32[f]	original	2D		88 (3) 63 (5)[g]		73 (6) 96 (12)		-41 (6) -12 (6)		32 (5) 25 (10)
Li	2013	64	46	original	3D	61 (2)[g]	60 (2)	195 (7)	167 (8)	-13.4 (8)	-12.8 (9)	23 (3)	27 (3)
Carrington	2014	19	96	original	2D	73 (23)[i]	65 (19)	144 (116)	113 (62)	n.r.	n.r.	16 (33)	24 (22)
Lee	2014	27	27	original	3D	46 (39-65)[j]	32 (24-42)	55 (41-77)	20 (12-28)	30 (5-66)	15 (5-30)	16 (0-82)	30 (0-75)
Sauter	2014	11	17	original	2D	109 (26)[a]		153 (92)		-44 (22)		n.r.	
Xu	2014	34	37	original	3D	63 (2)[a,e]		183 (7)		-21 (6)		26(3)	
Coss-Adame	2015	36	42	original	3D	90 (83-96)[k]	76 (71-81)	151 (120-182)	104 (82-127)	n.r.		n.r	

a. Male and female data reported together
b. Data reported as median (range)
c. Data reported in cmH_2O
d. n.r. = not reported
e. Women aged <50 years
f. Women aged >50 years
g. Data expressed as mean (SEM)
h. data reported as maximum absolute squeeze pressure
i. Data expressed as mean (SD)
j. Data expressed as median (IQR)
k. Data expressed as mean (95% CI)

Table 3-I Table summarizing results of studies that report traditional measures of anorectal function using high-resolution anorectal manometry (HRAM). Results are for average anal resting pressure and incremental squeeze pressure unless stated otherwise.

Within these studies, cohort sizes range from 28 (Sauter et al., 2014) to a maximum of 115 (Carrington et al., 2014a).

In general, there is reasonable concordance between studies with regard to average values reported for anal resting tone, aside from a Korean population study (Lee et al., 2014), where resting pressure was significantly lower, most notably for females, and also a Swiss study, where anal resting tone was markedly higher (Sauter et al., 2014). Whether this is due to true differences in populations investigated, or to variations in methodology (e.g. catheter-type, analysis algorithms etc.) is unclear. Generally, those recorded with the 3D HDAM catheter (Xu et al., 2014, Coss-Adame et al., 2015) are higher; this has been attributed to the relative thickness of the rigid probe (2–3 times thicker than HRAM catheters), which may induce stretch of the external anal sphincter, resulting in a higher contraction force (Coss-Adame et al., 2015).

Consistent with previous literature, some studies found a significant difference in absolute values between males and females (Lee et al., 2014, Carrington et al., 2014a) and one found differences associated with participant age (Noelting et al., 2012). One study reported differences in anal squeeze increment between parous and nulliparous females but did not find an association with age (Carrington et al., 2014a). A further study reported a positive correlation between BMI and anal resting pressure and the rectoanal gradient (Lee et al., 2014).

A further study investigated anal canal length, resting tone and parameters of the recto-anal inhibitory reflex using water-perfused HRAM in 180 newborns, and showed that resting tone is higher in those born at term than preterm, and that there is progressive maturation of sphincter pressures with increasing age which stabilized at around 1 month. Anal canal length did not vary by gestational age. The rectoanal inhibitory reflex (RAIR) was elicited in all subjects (Tang et al., 2014).

3.4.3 Comparison with traditional techniques

Of the 4 articles that describe a comparison between HRAM and CAM, three used HRAM and one used 3D HRAM / HDAM. All papers compared anal resting pressure and squeeze pressures and 3 described data pertaining to manoeuvres of rectoanal co-ordination. These data are summarized in Table 3-II.

Two of the 4 papers reported consistently higher absolute values for both (or either) resting and squeeze pressures (Jones et al., 2007, Vitton et al., 2013d) however both these studies compared water-perfused CAM and solid-state HRAM, raising the possibility that differences in absolute values could be secondary to the method of data collection and not due to differences in manometric resolution / analysis technique.

The remaining two articles derived traditional values via a subsampling technique of data collected using a HRAM system (Sauter et al., 2014, Soubra et al., 2014). Neither of these articles reported a difference between absolute anal resting and squeeze pressures.

All studies reported good correlation of values between techniques (interclass correlation coefficients (ICC) ranging from 0.42 – 0.9) (Jones et al., 2007, Vitton et al., 2013d, Sauter et al., 2014). An article that derived values through subsampling reported the highest ICC (Sauter et al., 2014) suggesting that the HRAM method of results analysis has little absolute effect on the reporting of traditional measures of anal function.

Author	Year	*N*	Article type	Participants	CAM type	2D/3D HRAM	Anal resting pressure (mmHg)				Anal squeeze pressure (mmHg)			
							HRAM	CAM	sig	ICC (*p*)	HRAM	CAM	sig	ICC (*p*)
Jones	2007	29	original	mixed[a]	WP	2D	54 (5)[c]	65 (5)	n.s.	0.51 (.002)	101 (9)	145 (12)	< .0001	0.78 (< .001)
Vitton	2013	201	original	mixed	WP	3D	73 (45)[d]	49 (23)	< .001	0.42 (< .001)	92 (58)	48 (24)	< .001	0.48 (< .001)
Sauter	2014	26	original	HV[g]	SS	2D	109 (26)[d]	108 (26)	n.r.	0.87 (n.r.)	153 (92)	143 (84)	n.r.	0.92 (n.r.)
Soubra	2014	25	original	DD[h]	n.r.	2D	70[h]	56	< .001	n.r. (n.r.)	131	122	n.s.	n.r. (n.r.)

a. mixed = mixed patient group
b. WP = water perfused
c. Data expressed as mean (SEM)
d. Data expressed as mean (SD)
e. SS = solid state
f. n.r. = not reported
g. HV = healthy volunteer
h. DD = dyssynergic defaecation
i. Data expressed as mean

Table 3-II Table summarizing results of studies that compare conventional anorectal manometry (CAM) and high-resolution anorectal manometry (HRAM). Results are for average anal resting pressure and incremental squeeze pressure unless stated otherwise.

3.4.4 Comparison with other tests of anorectal function

In 5 separate studies, results of HRAM / 3D HRAM have been compared with the findings of other allied investigations of anorectal structure/function, namely defaecography, magnetic resonance (MR) defaecography, endoanal ultrasound and 3D transperineal ultrasound.

With regard to assessment of evacuatory function, one recent study (Heinrich et al., 2015) reports high accuracy for the diagnosis of dyssynergia using HRAM in patients shown to have dyssynergia on MR defecography. Additionally, specific manometric patterns were seen in patients with an intra-anal intussusception on MR imaging, suggesting than HRAM can accurately diagnose some patients with either 'functional' or 'structural' causes of their evacuatory difficulty.

By contrast, Jodorkovsky et al. (Jodorkovsky et al., 2014) were unable to find a correlation between 3D HRAM findings and structural pelvic defects on MR defecography (aside from a weak correlation between intrarectal pressure at rest and rectocele size and organ prolapse), and concluded that 3D HRAM could not be used to predict anatomical abnormalities.

Benezech *et al.* performed comparison of 3D HRAM with conventional defaecography. The study described 19 patients with excessive perineal descent as determined by conventional defaecography (in the sitting position) who underwent HRAM (in the left lateral position). They demonstrated that the mean perineal descent was significantly less when measured with HRAM than conventional defaecography, despite a reasonable correlation between the two techniques. The authors suggested that the variance in absolute values might be explained by differences in patient positioning (Benezech et al., 2014).

Vitton et al. assessed the ability of 3D HRAM to identify anal sphincter defects by comparison of findings with endoanal ultrasound (taken as the gold standard) in 100 consecutive patients (Vitton et al., 2013a). For the identification of internal anal sphincter defects, a sensitivity of 86% and specificity of 59% was reported for 3D HRAM, whereas for external anal sphincter defects, there was a sensitivity of 79% and specificity of 70%.

In a study of healthy subjects, Raizada et al. (Raizada et al., 2011) showed that anal canal length as measured by 3D HDAM was slightly longer than when measured by 3D transperineal ultrasound, which was attributed to the limited discriminant ability of HDAM transducers to accurately assess short (<4 mm) distances.

3.4.5 Additional / improved clinical utility

Although HRAM and 3D HRAM/HDAM methods now exist, the question as to whether they actually provide improved clinical utility over traditional manometric methods needs addressing to determine if they are indeed diagnostically superior, or simply a refinement of existing techniques.

From the most basic perspective, color contour/ topography plots provide a dynamic and continuous representation of anorectal pressure information, which is both more visually arresting and intuitive compared to traditional line plots. Furthermore, the color topographic display allows for better appreciation of catheter movement relative to the anorectum. Sauter et al. (Sauter et al., 2014) have suggested that complete relaxation of the anal sphincter recorded by standard manometry during simulated defecation is often artefactual, caused by movement of pressure sensors out of the anal sphincter during abdominal straining; they showed that such a shift in catheter position, sufficient to produce an artefactual 'relaxation' on at least one pressure sensor occurred in 68/123 (55%) 'push' maneuvers (Figure 3-II).

In terms of procedure time, two reports indicate that performing an HRAM study is ~12 min quicker than performing a traditional anorectal manometry study

(Sauter et al., 2014, Kang et al., 2015) although study duration is (to some extent) clearly dependent upon the complexity of the protocol undertaken.

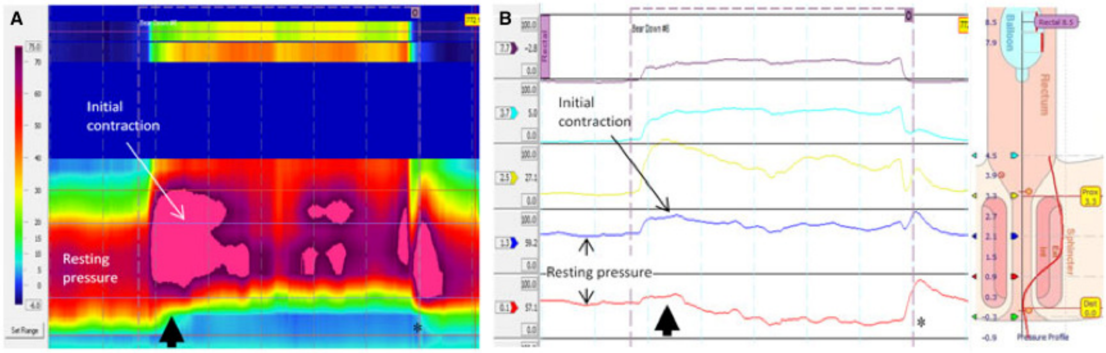

Figure 3-II Figure and legend reproduced from Sauter *et al.* 2014. A) High-resolution pressure topography and (B) conventional line plots in a healthy volunteer. The apparent drop in sphincter pressure with anal sphincter relaxation on conventional line plots (black arrow on Fig. 1B) is due to downward movement of the catheter relative to the anal sphincter. Catheter position returns into position after straining has ceased (Asterix*) (Sauter et al., 2014).

3.4.6 Novel features of functional anatomy

One apparent advantage of HRAM, and particularly 3D HRAM/HDAM, is the ability to exquisitely define functional anatomy of the anal canal. Due to its relatively short length, its proximity to the distal rectum, and movement that occurs during events such as squeeze and push, traditional manometry utilizing single-point pressure sensors has proven to be an inadequate technique to define functional anatomy with adequate resolution.

Four studies utilised HRAM to appreciate novel features of anorectal function. Three studies utilised 3D HRAM in adult participants. One study utilised 3D HRAM in children with constipation.

The functional morphology of the anal sphincter was examined in detail in a study of 15 nulliparous women with 3D HRAM, 3D ultrasound and dynamic MR.

Colour contour plots demonstrated asymmetry of the anal canal both axially and circumferentially. In addition they report that the functional length of the anal canal as measured by 3D HRAM is slightly shorter than the morphological length as measured by 3D ultrasound. The authors suggested that these findings are related to the contribution of puborectalis and the external anal sphincter to proximal and distal anal canal pressures, respectively (Raizada et al., 2011).

Anorectal functional anatomy was also explored in a study of 30 children with constipation. The authors reported that following adjustment for sphincter length, the peak intra-anal pressure was located at a distance of 36% of the anal canal from the anal verge at rest. Similar to the study by Raizada above, the authors also demonstrated asymmetric pressure distribution within the anal canal. (Ambartsumyan et al., 2013).

3D HDAM has also yielded more precise information regarding the functional anal response to rectal distension (RAIR). A study in 10 healthy volunteers demonstrated that increased volume of rectal distension induces an increasingly profound and prolonged inhibition of anal sphincter tone. Most marked relaxations were seen in the superior-posterior position leading the authors to suggest that this reflected relaxation of both puborectalis and the internal anal sphincter. At high inflation volumes pressures remained high within the distal anal canal. The authors suggested that this confirmed lack of external anal sphincter contribution to the reflex (Cheeney et al., 2012).

A further manuscript by the same group investigated the characteristics of the sensorimotor response (SMR) (the transient anal contraction seen overlying the initial relaxation phase of the RAIR). Three-dimensional HRAM was utilised in 10 healthy volunteers and rectal balloon distensions performed up to either maximum toleration or 320mls. They used 3D pressure topography to demonstrate that the pressure increase seen during the SMR corresponded to the anatomical location of the posterior fibres of puborectalis (Figure 3-III). The authors suggested that the study was only possible due to the unique spatiotemporal resolution of 3D-HRAM (Cheeney et al., 2011).

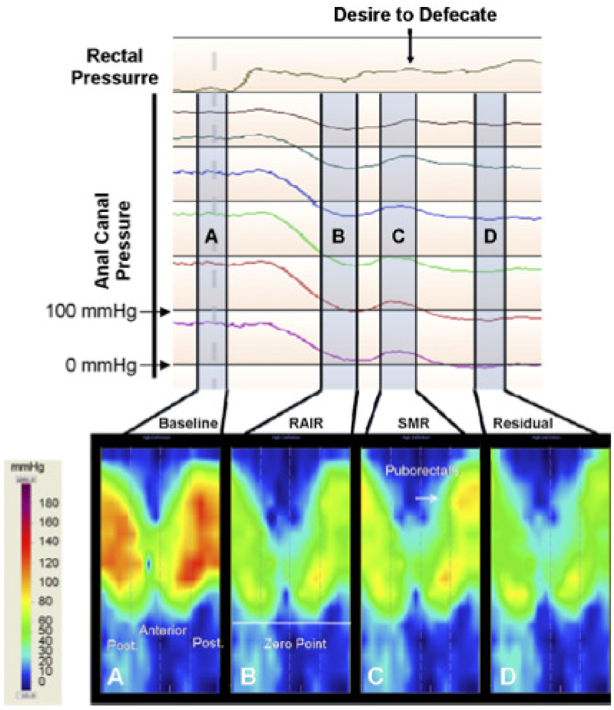

Figure 3-III Figure from Cheeney *et al.* 2011 demonstrating manometric line traces and high-resolution topographic pressure profiles taken before, during and after a sensorimotor response in a single subject (Cheeney et al., 2012).

3.4.7 Utility in defaecatory disorders

Manometry (together with the balloon expulsion test) has been recommended by some as the initial test of choice to assess patients with defecatory disorders (American Gastroenterological et al., 2013) although others advocate defecography (either barium or MR) if resources allow (Lindberg et al., 2011) Defecatory disorders may be caused by 'functional' or structural anorectal disturbances that may coexist.

Four subtypes of dyssynergia seen with traditional manometry have previously been proposed by Rao et al. (Rao et al., 2004). Using HRAM technology, Ratuapli et al. have attempted to refine this classification (Ratuapli et al., 2012). They studied 62 healthy females and 295 females with constipation, and used a principal components analysis of rectoanal pressures to construct phenotypes associated with prolonged balloon expulsion time.

They demonstrated that 3 phenotypes, and were able to discriminate between patients with normal and abnormal BET. The authors report 75% specificity and 75% sensitivity for a principal components model to distinguish between healthy subjects with a normal BET, and controls/patients with a prolonged BET. However, the clinical utility of such a complex method of analysis is questionable. This study also showed that a negative rectoanal pressure gradient during push (which is considered indicative of a defecatory disorder), was an almost universal finding, even in the control subjects. (Ratuapli et al., 2012). These findings have since been reproduced by others (Sauter et al., 2014, Coss-Adame et al., 2015), which brings into considerable doubt the diagnostic utility of this variable.

Coss-Adame et al. (Coss-Adame et al., 2015) reported that 67% of healthy subjects (12/18) showed a dyssynergic pattern during attempted defecation. Sauter et al. (Sauter et al., 2014) reported that only 4 of 25 healthy subjects (16%) had the 'expected' positive rectoanal pressure gradient during the bearing down maneuver on HRAM. The authors provided an explanation for the finding of a higher anal pressure than rectal pressure during the 'push' maneuver, in that the force of (simulated) defecation drives the recording catheter against the wall of the anal canal, thus producing a 'contact' pressure high enough to produce a negative pressure gradient (Sauter et al., 2014).

Most recently, Grossi et al. (Grossi et al., 2015) have shown that blinded assessment of anorectal pressures (from HRAM traces) during simulated defecation in 170 subjects (85 controls, and 85 patients with functional constipation) disclosed a 'normal' pattern in only 13% of healthy volunteers (and only 6% of patients), suggesting that manometric evaluation of push maneuver may be of limited utility for discriminating between health and disease. These findings reinforce the need to re-evaluate the role of manometry for diagnosing dyssynergia.

3.4.8 Utility in faecal incontinence

To date, no published study has been solely performed in patients with fecal incontinence. Of those series in which patients with incontinence were included (Jones et al., 2007, Heinrich et al., 2013, Vitton et al., 2013d, Vitton et al., 2013a, Kang et al., 2015) no improvement in clinical utility for HRAM methods has thus far been demonstrated.

3.4.9 Novel HRAM metrics

Two manuscripts describe novel methods of analysis of data from HRAM during the assessment of anal sphincter function. One utilised 3D HRAM and the other 2D HRAM.

Apart from the previously described novel phenotypic classification system proposed by Ratuapli et al. (Ratuapli et al., 2013c), one further study has described a novel method for describing anorectal function by applying the concept of an integrated pressure volume (IPV) calculation (commonly used to determine the distal contractile integral during oesophageal HRAM) during attempted defaecation. In 54 healthy volunteers the push maneuver was assessed using 3D HRAM in the left lateral position and compared to balloon expulsion times. A 3D IPV comparing pressure ratios between the distal rectum and proximal anal canal during push was found to predict balloon expulsion results (Jung et al., 2014). Whether this novel methodology is applicable to the study of patients with defaecatory disorders remains unclear.

Qualitative assessment of HRAM colour contour plots also appears to display findings previously unrecognized with conventional manometry (Carrington et al., 2014a, Sauter et al., 2014). One paper described qualitative findings of the colour contour plots (Carrington et al., 2014a). Images of 3 individuals with similar absolute values for squeeze appeared heterogeneous on inspection of the anal sphincter as a global unit (Figure 3-IV). The authors suggested that further area of investigation of the importance of squeeze morphology might prove useful.

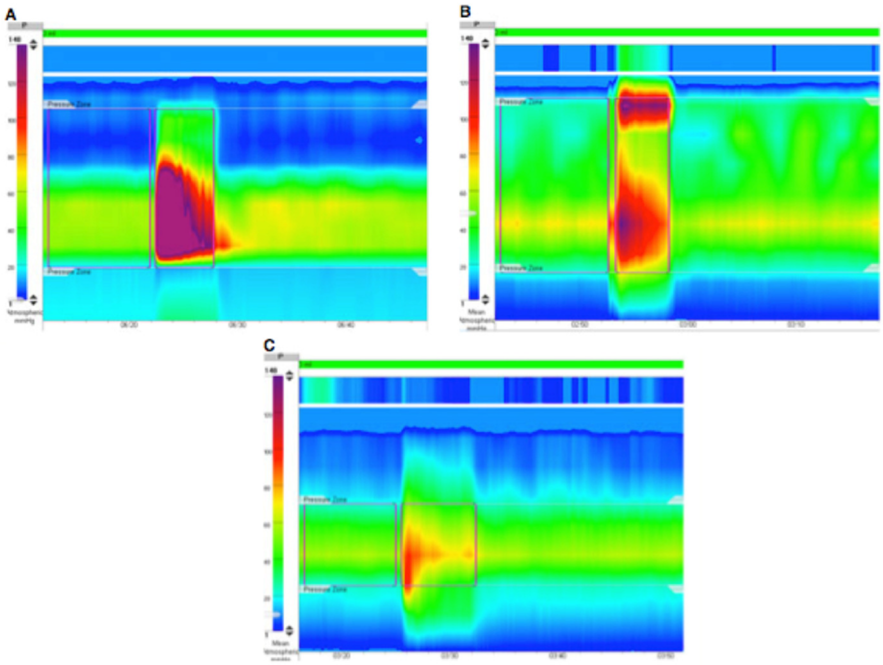

Figure 3-IV Figure modified from Carrington *et al.* 2014 demonstrating the heterogeneity of squeeze morphology in health. (A) Contribution from the whole anal canal; (B) increase in anal canal pressure showing two distinct high pressure zones, (C) increase in anal canal pressure predominantly secondary to presumed contraction of the distal external anal sphincter (Carrington et al., 2014a).

3.5 Discussion

This review includes all full-text manuscripts describing data obtained using HRAM and 3D HDAM without exclusion on the basis of study design and protocol. Regrettably, the majority of data have been derived from low quality human studies – exploratory case series without sample size analyses, many of which describe data which were likely collected retrospectively and will therefore have suffered from selection and performance bias.

Nevertheless, the data support the notion that data obtained using HRAM is at least as acceptable as and indeed comparable to traditional techniques. Some studies suggest that computer derived quantitative measures of function may be different to those found using conventional manometry, however methodological difficulties (the use of alternate manometric systems) limit the usefulness of these data. Studies that use a subsampling technique to derive CAM data from HRAM probes suggest similarity in absolute values of traditional measures of anorectal function.

One apparent advantage of HRAM is the ability to exquisitely define functional anatomy. Three-dimensional definition of the anorectum has previously been performed with vector-volume manometry, however high resolution technology has the significant advantage of being able to image the whole anal canal simultaneously instead of utilizing a rapid pull through technique, allowing for a more global and 'real time' assessment of activity such as the RAIR.

In addition, due to the small size of the anal canal, its proximity to the distal rectum, and movement that occurs during events such as squeeze and push, single point pressure sensors utilised with traditional manometry are unable to give information with enough resolution to appreciate coordinated events. The application of 3D HRAM in this setting has demonstrated previously unrecognized features of anal function such as the contribution of puborectalis to the SMR.

However, whether such applications are useful clinically remain to be proven. To date there are no studies within the published literature which conclusively demonstrate a clinical, diagnostic or interventional advantage of HRAM over traditional techniques. Such evidence will be required prior to generalized introduction of this technique.

Within the more established oesophageal literature, the opinion is that utilization of the high-resolution manometric technique is beneficial due to simpler recognition of normal and abnormal function with colour-contour plots, quick and easy positioning of the catheter, decreased study time and improved ability to recognize inadvertent catheter movement (Fox et al., 2004). It is likely that such advantages will hold true during application to the anorectum, however whether or not these advantages outweigh the problem of expensive equipment and lack of current expertise remain to be seen. Ultimately, more prospective research establishing the clinical benefits of HRAM is required prior to recommendation of these techniques over and above existing methods.

3.5.1 Methodological limitations

The following methodological limitations are acknowledged. First, although PRISMA guidelines for methodology were followed, for reasons of practicality during manuscript review, the investigator was not blinded to institution, author or journal title.

Secondly, as the author has a particular interest in HRAM, it is likely that there may have been some impact on objectivity when reporting results from allied institutions.

Third is the lack of inclusion of data presented in abstract format. Due to the emerging nature of this technique, much pertinent data is still to be published in full-text format. Due to difficulty in scrutinizing methodology and understanding data in context, the balanced decision was to exclude studies published in abstract form only. It is however acknowledged that this review is likely lacking some data of interest.

3.5.2 Implications of this study

This review has exhibited the current data pertaining to HRAM. It has confirmed that HRAM has a place in understanding the functional anatomy of the anorectum and has presented some novel metrics of coordinated rectoanal activity, which may be of diagnostic value.

Ultimately more research establishing the clinical benefits of this technique is required prior to recommendation of this technique over and above conventionally accepted methodology.

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Chapter 4

4 Development and validation of a standardised protocol for high resolution anal manometry

4.1 Rationale

As established in earlier chapters of this thesis, the practice and interpretation of anal manometry is plagued by a lack of standardization. There is no consensus with regard to either the optimal test protocol or method of reporting, despite several position statements and working party reports being published on the topic (Keighley et al., 1989, Barnett et al., 1999, Azpiroz et al., 2002, Rao et al., 2002). This has created significant difficulty in comparison of results between centres, both clinically and in the research setting.

Despite a number of reasonably sized normative datasets within the literature (most of which pertain to conventional manometry) (Cali et al., 1992, Chaliha et al., 2007, Gundling et al., 2010, Noelting et al., 2012, Schuld et al., 2012), to the author's knowledge there is no study outlining the impact of protocol technique (i.e. impact of familiarization period, ideal resting period, optimal manoeuvre number) on results reporting. It is therefore likely that current practice is dictated solely by expert opinion and institutional preference.

Even so, as anal manometry is a dynamic investigation partly of voluntary function, it is well appreciated that nuances of study protocol are likely to impact derived results (Schouten and van Vroonhoven, 1983, Rao et al., 1999, Rao et al., 2002, Heinrich et al., 2013). Indeed, a recent study in 70 patients with defaecatory dysfunction demonstrated that enhanced instruction and verbal feedback significantly improved squeeze pressures when compared to standard instruction (Heinrich et al., 2013). Likewise, it seems reasonable to postulate that the performance of repeated manoeuvre attempts (e.g. squeeze or cough) may affect final results. This is likely to be particularly pertinent during application of studies to patients with underlying pelvic floor and sphincter dysfunction, in whom voluntary control is significantly reduced.

4.2 Aims

The general aim of this pilot study was to develop and define the optimal investigation protocol for HRAM.

The specific aims of this study were:

1. To define the optimal familiarisation period required prior to measurement of anal resting pressure
2. To define the ideal number of manoeuvres for squeeze, endurance squeeze, push and cough required to obtain a consistent result
3. To define (if required) the necessary between-manoeuvre interval required to allow for recovery of baseline anal function

4.3 Methods

Healthy, asymptomatic male and female subjects were recruited at Barts and the London School of Medicine and Dentistry, London. Ethical approval was granted by the Queen Mary University Research Ethics Committee (ref QMREC 2010/74 and QMREC 2013/12), and written informed consent obtained. A general and focused clinical history and examination was performed in all participants using a standardised methodological approach.

Subjects were recruited on the basis of local advertisement and were reimbursed £50 for time and travel. Exclusion criteria were (1) current or previous history of significant faecal incontinence of constipation (2) current or previous history of neurological disease (3) current use of medications that could potentially influence anal function (4) history of anorectal surgery or trauma (5) inability to provide informed consent for the study (6) inability to communicate effectively in English.

Subjects underwent an initial screening interview during which they were asked a set of standard questions based on the exclusion criteria above. On the study day subjects underwent a full general and focussed clinical history following a standard proforma (see Appendix C). This included the completion of the St Marks Faecal Incontinence Score (Vaizey et al., 1999) and a Cleveland Clinic Constipation Score (Agachan et al., 1996). Any subject who scored >4 on the SIMS score or >7 on the CCCS was excluded from the study. If at this time the participant was found to fulfil any of the other exclusion criteria at this time they were also excluded from to the study. The subjects used in this chapter formed the first 50 individuals recruited for chapter 5. A further description of exclusions with a CONSORT diagram is available in section 5.3.1.

HRAM was performed using a solid-state catheter (UniTip: UniSensor AG, Switzerland), of external diameter 12 F, incorporating 12 microtransducers, each of which measured circumferential pressure by means of a pressure sensor embedded within silicone gel. Ten of these sensors were spaced 0.8 cm apart, spanning 7.2 cm. The most proximal microtransducer was located within a non-latex balloon 3.3 cm proximal to these. The most distal sensor (located 2 cm below the most distal of the central 10 sensors) was used as an external reference (Figure 4-I).

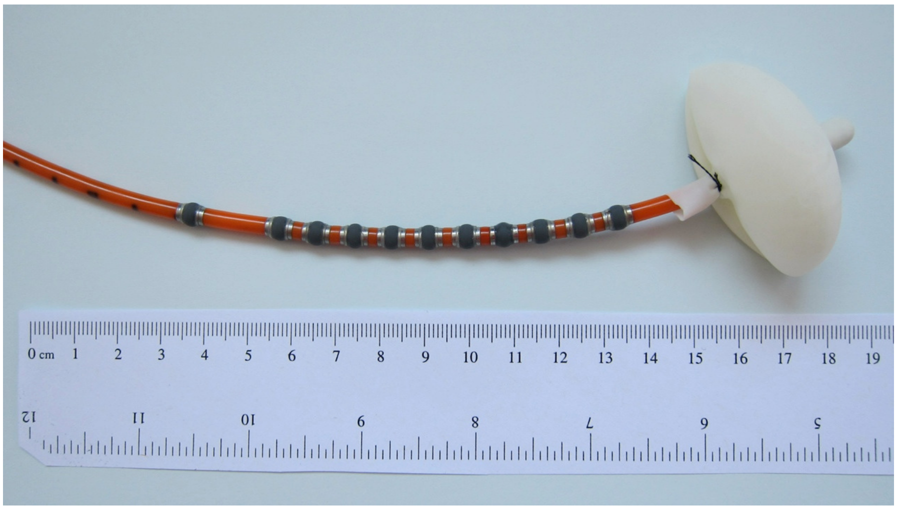

Figure 4-I Photograph of solid state HRAM catheter (UniTip: UniSensor AG, Switzerland).

Before every study, the catheter was immersed in tepid water for at least 3 minutes to pre-wet the sensors. Sensors were then zero-ed to atmospheric pressure under 1cm of water according to manufacturers guidelines. Data acquisition, online visualization and signal processing were performed using a commercially available manometric system (Solar GI HRM v9.1, Medical Measurement Systems (MMS), Enschede, Netherlands).

All test manoeuvres were performed in accordance with published guidelines (Rao et al., 2002). Immediately before study onset, a digital rectal examination was performed during which the participant was asked to 'squeeze' and 'push' allowing the investigator to assess understanding of these commands. If the participant failed to perform these manoeuvres adequately, they were briefly given further instruction and encouragement.

To perform the study, the catheter was inserted into the anorectum with the distal 2 microtransducers visible (the second most distal being located immediately outside of the anal verge). Following insertion of the catheter the following manoeuvres were performed with a 30 second recovery period between each manoeuvre:

1. five-minute period of rest
2. 5 x five-second voluntary squeeze manoeuvres

3. 2 x thirty-second endurance squeeze manoeuvres
4. 2 x push manoeuvres
5. 2 x cough manoeuvres

For each manoeuvre, the anal canal area was highlighted using software's e-sleeve tool (Figure 4-II). This allowed the software to derive the maximum pressure recorded over this area of interest at each point in time (sampling rate 10 Hz).

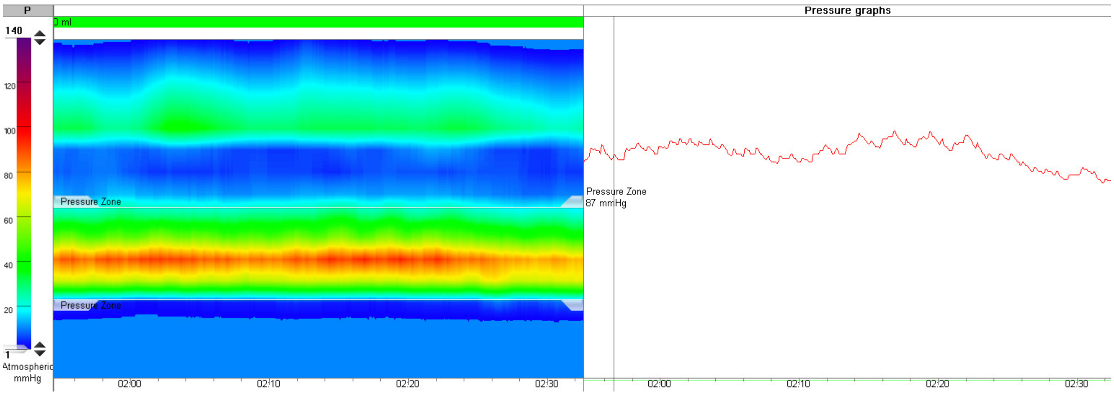

Figure 4-II Colour contour plot and corresponding line trace of anorectal pressures at rest demonstrating the e-sleeve pressure zone.

Results were calculated automatically over the duration of the manoeuvre using in-built software analysis tools. The following data were captured:

Average anal resting pressure

This was defined as the average maximum pressure (mmHg) over the functional anal canal length during the 1-minute period of rest.

Average incremental squeeze pressure

This was defined as the mean maximum pressure (mmHg) that the volunteer was able to sustain over the duration of the 5 second squeeze manoeuvre minus the mean maximum resting pressure prior to the manoeuvre (over 5 seconds).

Endurance squeeze duration

This was defined as the length in time (sec) over which the subject was able to sustain a pressure at or above 50% of the highest recorded squeeze pressure (Rao et al., 2002). The endpoint was determined as the point at which the pressure first dropped below this threshold (Figure 4-III).

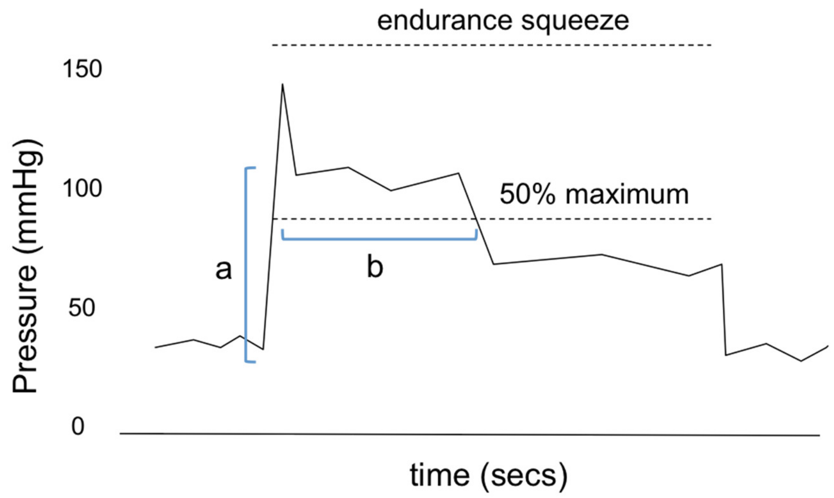

Figure 4-III Representative diagram of parameters measured during the endurance squeeze manoeuvre. (a) = sustained incremental endurance squeeze pressure; (b) = endurance squeeze duration.

Sustained incremental endurance squeeze pressure

This was defined as the mean maximum pressure (mmHg) that the volunteer was able to sustain over the duration of the 30 second endurance squeeze manoeuvre minus the mean maximum resting pressure prior to the manoeuvre (over 30 seconds) (Figure 4-III).

Residual anal push pressure

This was defined as the lowest maximum pressure (mmHg) recorded within the anal canal over the duration of each 5-second push manoeuvre.

Maximum absolute anal cough pressure

This was defined as the highest recorded pressure within the anal canal (mmHg) at any point during each cough manoeuvre.

4.4 Data analysis

To allow analysis of changes in resting pressure over time (and thence determine the minimal familiarisation period), data from the 5-minute period of rest was divided into ten 30-second epochs, each of which was analysed separately and compared by repeated measure analysis of variance (RM-ANOVA).

To examine consistency over the remaining repeated measures, repeat manoeuvres were analysed with intraclass correlation statistics, Bland-Altman plots, RM-ANOVA or paired t-tests as appropriate. Statistical analysis was performed using IBM SPSS Statistics version 20. Significance was set at $p < .05$.

4.5 Results

4.5.1 Subjects

A total of 50 volunteers were recruited for the study (11 males, 39 females; median age 38 [range 21 – 68] years). All subjects tolerated the procedure without complication. Recruitment was weighted towards parous females (22/39 females), as this is representative of the patient cohort that usually present for assessment of anal sphincter function (Pretlove et al., 2006, Whitehead et al., 2009a).

4.5.2 RM-ANOVA: Definition of minimal familiarisation period required for stabilisation of anal resting pressures

Mean anal resting pressures for each 30-second epoch are displayed in Table 4-I.

A one-way repeated measures ANOVA was performed to compare this mean resting pressure across all ten 30-second intervals (time), to assess if resting pressure decreased significantly and consistently over time. Greenhouse-Geisser Epsilon statistics are reported, with adjusted degrees of freedom, where Mauchly's assumption of sphericity has been violated. Over this 5-minute period, there was a main effect for time (F (2, 108) = 27.55, p < .001, η2 = .37, medium effect size). A follow-up 2 (time) x 2 (sex) repeated measures ANOVA found no significant interaction effect of time x sex on resting pressure (F (2, 104) = .606, p = .571), suggesting no separate cut-off points for males and females are needed (Figure 4-IV).

Descriptive Statistics

Mean resting pressure (mmHg)	Mean	Std. Deviation
0:00 - 0:30 mins	86	25
0:30 - 1:00 mins	81	24
1:00 - 1:30 mins	78	24
1:30 - 2:00 mins	74	22
2:00 - 2:30 mins	74	24
2:30 - 3:00 mins	71	22
3:00 - 3:30 mins	70	23
3:30 - 4:00 mins	69	22
4:00 - 4:30 mins	68	24
4:30 - 5:00 mins	68	24

Table 4-I Table of descriptive statistics for mean anal resting pressures (mmHg) during 10 consecutive 30-second periods.

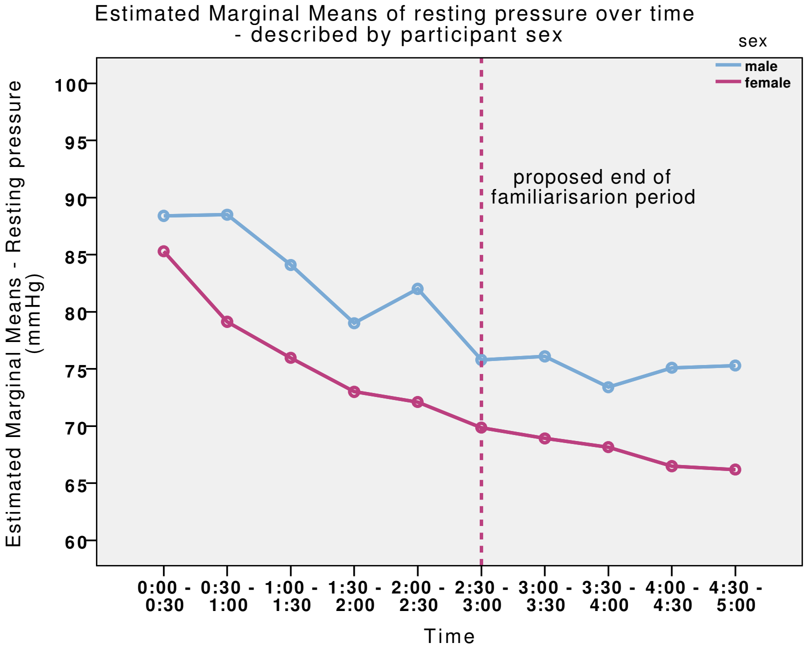

Figure 4-IV Line graph of estimated marginal means demonstrating changes in anal resting pressure over time in male (light blue) and female (pink) participants.

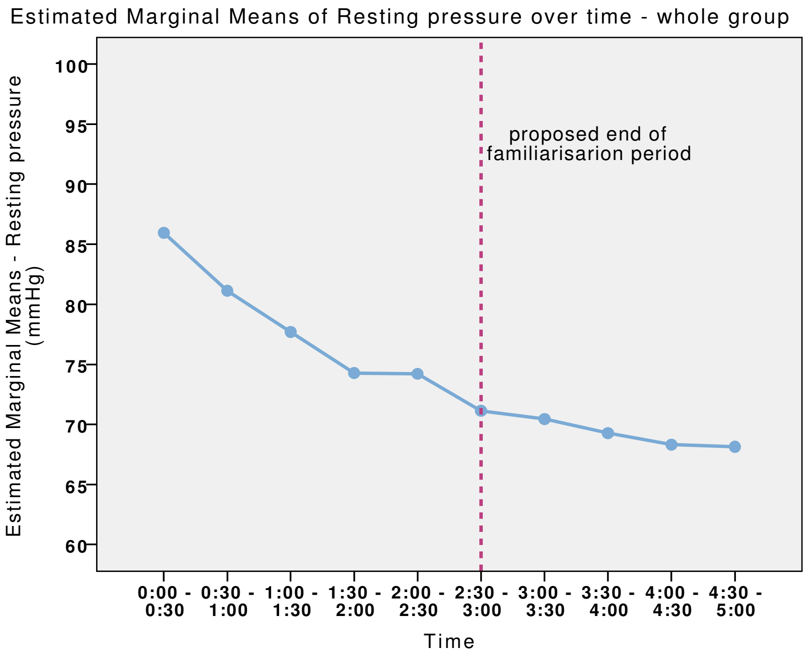

Figure 4-V Line graph of anal resting pressure estimated marginal means for whole group. Dotted pink line indicates proposed end of familiarisation period.

Visual inspection of mean resting pressure over time (Figure 4-V) intimated that following the initial downward trend, anal pressures appeared to stabilise at around 3 minutes. A final one-way repeated measures ANOVA was performed to compare mean resting pressure across the final four (consistent) time intervals (from 3:00 – 5:00 minutes). This analysis confirmed that within this 2 minute time period, there was no main effect of time on resting pressure ($F(2, 100) = 2.64$, $p = .071$).

4.5.3 RM-ANOVA: Determination of the minimum number of squeeze manoeuvres required to achieve a consistent response

Similarly, mean average incremental squeeze pressures for all squeeze attempts in the whole group, males and females are displayed in Tables 4-II, 3-III and 3-IV. Inspection of data from the group as a whole suggested markedly lower pressures for squeeze 2 than other squeeze attempts. Division of data into male and female subgroups and depiction as a line graph of estimated marginal means (Figure 4-VI) demonstrated that this was secondary to excessive increments for the first squeeze manoeuvre in males.

Descriptive Statistics (whole group)

Average incremental squeeze pressure (mmHg)	Mean	Std. Deviation
Squeeze 1	134	73
Squeeze 2	126	63
Squeeze 3	133	73
Squeeze 4	128	71
Squeeze 5	128	67

Descriptive Statistics (males)

erage incremental squeeze pressure (mmHg)	Mean	Std. Deviation
Squeeze 1	165	68
Squeeze 2	141	59
Squeeze 3	138	72
Squeeze 4	134	65
Squeeze 5	134	58

Descriptive Statistics (females)

Average incremental squeeze pressure (mmHg)	Mean	Std. Deviation
Squeeze 1	126	74
Squeeze 2	122	65
Squeeze 3	132	75
Squeeze 4	126	74
Squeeze 5	127	70

Tables 4-II, 4-III and 4-IV showing mean incremental squeeze pressures during each of 5 squeeze attempts for the whole group, males and females respectively.

A one-way repeated measures ANOVA was performed to compare mean average squeeze increment over all five 5-second squeezes (attempts), to assess if squeeze pressure changed significantly and consistently during repeated attempts. Once again, Greenhouse-Geisser Epsilon statistics are reported, with adjusted degrees of freedom, where Mauchly's assumption of sphericity has been violated. Over these 5 attempts, there was no main effect for attempts ($F(2, 57) = .870$, $p = .423$).

Despite this, inspection of absolute values suggests markedly elevated values for the first attempt in males. Further review of data divided by sex suggested that following the initial high first squeeze increment in males values appeared to stabilise after the second attempt (Figure 4-IV). This was confirmed when a further one-way repeated measures ANOVA was performed to compare average incremental squeeze pressure across the final four (consistent) squeeze attempts (squeezes 2 - 5). This analysis confirmed that within these 4 squeezes, there was no main effect of attempts on squeeze pressures ($F(2, 52) = .269$, $p = .749$).

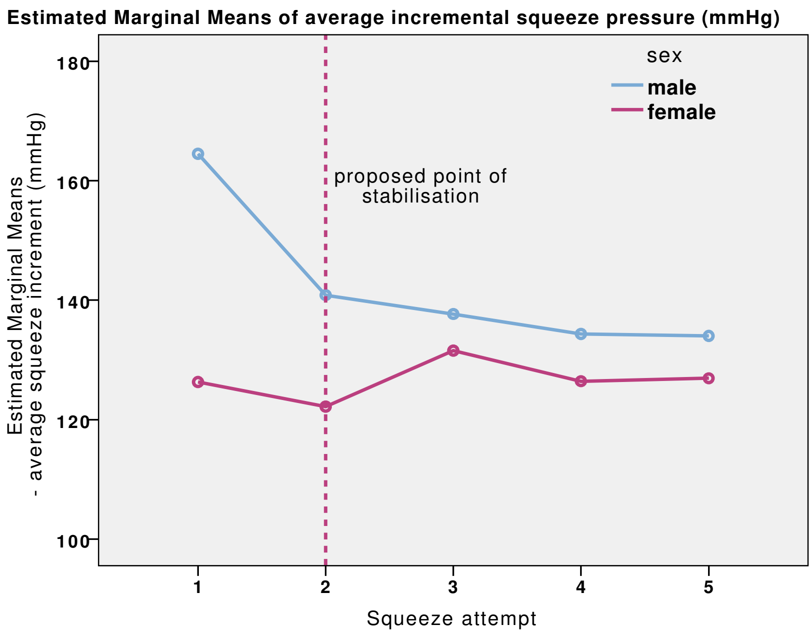

Figure 4-VI Line graph of estimated marginal means during 5 squeeze attempts in male (light blue) and female (pink) participants.

4.5.4 Paired t-test: Comparison of repeat attempts of endurance squeeze

A paired-samples t-test was used to examine whether there was a significant difference in endurance squeeze duration between the first and second endurance squeeze attempts. Average duration for the first attempt (13.8 ± 11.5 seconds) was marginally shorter than for the second attempt (15.8 ± 23.4 seconds), however this difference (1.35 [95% CI -3.6 to .89] mmHg) was not statistically significant $t(38) = -1.222$, $p = .229$, $d = -.196$.

A 2-way, absolute agreement, intra-class correlation calculation was performed which revealed an ICC statistic of 0.91 (95% CI .82 to .95), F(38) $p < .001$. This suggested good consistency of repeated measures. Visual inspection of the corresponding Bland-Altman plot (Figure 4-VII) demonstrated that discrepancy between attempts was generally acceptable however for 5 individuals, difference between attempts was >10 seconds. There was no apparent trend of difference, nor alteration of variability with increased endurance squeeze time.

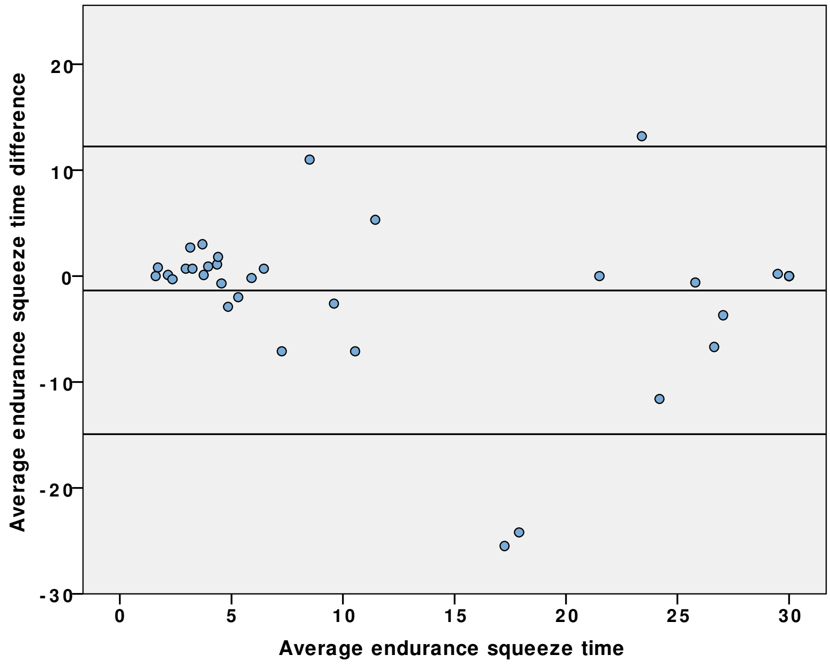

Figure 4-VII Bland-Altman plot describing difference between endurance squeeze time between attempts.

A further paired-samples t-test was used to examine whether there was a significant difference in average endurance squeeze increment between the first and second endurance squeeze attempts. Average increment for the first attempt (85 ± 49 mmHg) was slightly greater than for the second attempt (78 ± 46 mmHg), however this difference (6.5 [95% CI -.4 to 13.4] mmHg) was not statistically significant $t(39) = 1.907$, $p = .640$, $d = -.301$.

4.5.5 Paired t-test: Comparison of repeat attempts of the push manoeuvre

Similarly, a paired-samples t-test was used to assess whether there was a significant difference in residual push pressure between the first and second push manoeuvres. Residual push pressure for the first attempt (61 ± 29 mmHg) was near identical to that of the second attempt (59 ± 24 mmHg); this difference (1.7 [95% CI -1.2 to 4.6] mmHg) was not statistically significant $t(49) = 1.177$, $p = .275$, $d = .16$.

A 2-way, absolute agreement, intra-class correlation calculation for push residual pressure was performed which revealed an ICC statistic of 0.96 (95% CI .93 to .98), F(49) $p < .001$. This suggested excellent consistency of repeated measures.

Visual inspection of the corresponding Bland-Altman plot (Figure 4-VIII) demonstrated that discrepancy between attempts was generally acceptable however for 4 individuals, difference between attempts exceeded 20mmHg. There was a suggestion of a linear trend with pressure differences being higher in those with a higher average residual push pressure. Follow up linear regression modelling demonstrated that average residual push pressure explained 10.2% of the variance in differences between attempts ($F(1,48) = 5.444$, $p=.024$).

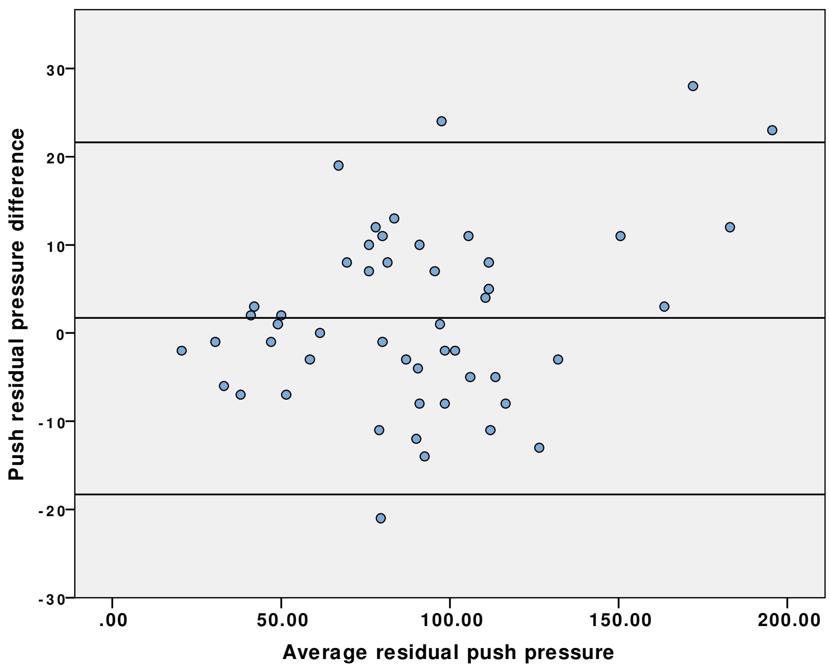

Figure 4-VIII Bland-Altman plot describing difference in push residual pressure between attempts.

4.5.6 Paired t-test: Comparison of repeat attempts of the cough manoeuvre

A further paired-samples t-test was used to elucidate whether there was a significant difference in the anal response to cough between the first and second cough manoeuvres. Maximum absolute anal cough pressure for the first attempt (202 ± 84 mmHg) was similar to that of the second attempt (197 ± 84 mmHg); this difference (5 [95% CI -3.2 to 13.1] mmHg) was not statistically significant $t(49) = 1.217$, $p = .229$, $d = .17$.

A 2-way, absolute agreement, intra-class correlation calculation for maximum absolute anal cough pressure was performed which revealed an ICC statistic of 0.97 (95% CI .95 to .98), F(49) $p < .001$.

This suggested excellent consistency of repeated measures. However inspection of the corresponding Bland-Altman plot demonstrated that there was quite marked discrepancy between individuals attempts, with 6 individuals demonstrating > +/- 50 mmHg between attempts, however all maximum cough pressures were greater than 120mmHg (Figure 4-IX). There was no alteration of variability with increased average pressure.

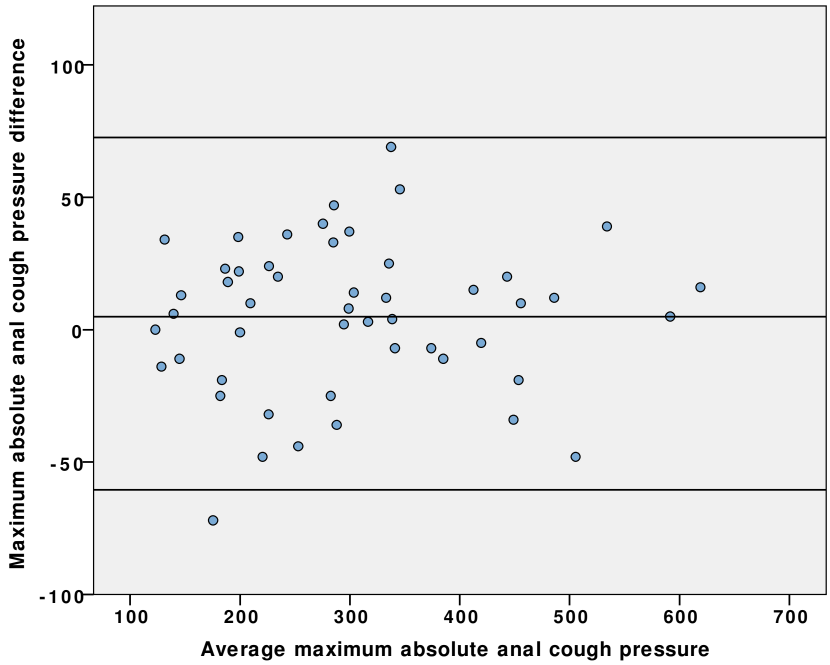

Figure 4-IX Bland-Altman plot describing difference between maximum absolute anal cough pressure between attempts.

4.5.7 Paired t-test: Comparison of anal resting pressures during between-manoeuvre intervals

Visual inspection of the colour contour plots during data collection suggested that following all manoeuvres, though most markedly the cough manoeuvres, there appeared, in some individuals, to be a transient post-manoeuvre reduction in anal resting pressure (Figure 4-X).

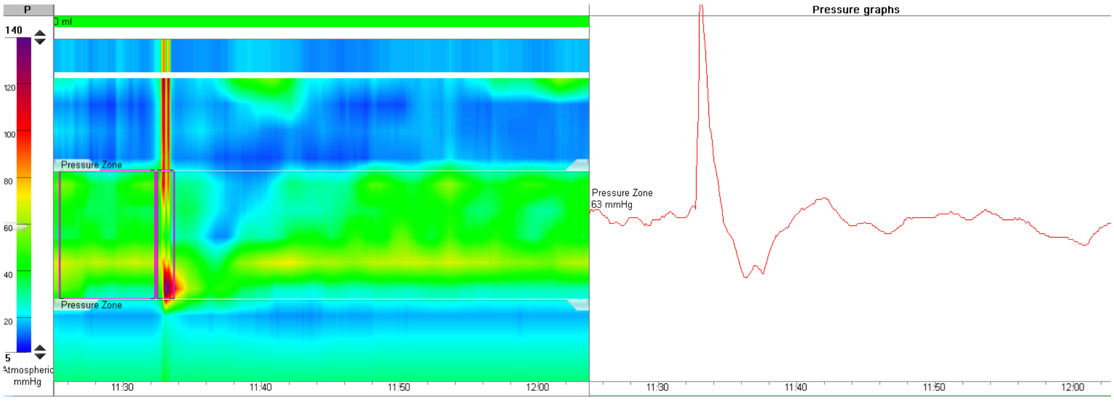

Figure 4-X Colour contour plot and corresponding line trace of a cough demonstrating transient post-manoeuvre reduction in anal pressure.

A paired-samples t-test was used to evaluate whether there was resolution of baseline anal pressures during the 30-second between-manoeuvre interval prior to onset of the next manoeuvre. Baseline mean anal resting pressure was compared with the mean anal resting pressure 10-seconds prior to the second cough attempt. This demonstrated that pressures at baseline (71 ± 25 mmHg) were near identical to those prior to onset of the cough (68 ± 24 mmHg); this difference (2.89 [95% CI -1.2 to 6.9] mmHg) was not statistically significant $t(46) = 1.427$, $p = .160$, $d = .20$.

4.6 Discussion

Analysis of results from this pilot extended HRAM protocol has demonstrated the following:

1. a need for a minimum 3-minute familiarization period to allow for stabilization of initially increased anal resting pressures;
2. no more than 2 squeeze and endurance squeeze attempts are required for consistent results
3. a 30-second between-manoeuvre interval is sufficient to allow for resolution of baseline anal pressures.

4. There may be significant variability in maximum anal cough pressures between attempts suggesting that an alternative method of measurement or alteration in measurement parameters may be useful.
5. In those individuals with high residual push pressures, there appears to be a trend towards a worsening result (i.e. higher residual pressure) with increasing attempts.

Although it appears reasonable that study protocol may affect results of anal manometry, to the author's knowledge, this is the first study that examines the effect of time on baseline anal resting pressure and compares differences between repeat manoeuvres of squeeze, push and cough.

As expected, initial resting pressures appeared falsely elevated, presumably secondary to uneasiness from anal intubation. A period of familiarisation within existing reported protocols is commonplace, however the length of this is variable and may last for up to 10 minutes (Felt-Bersma et al., 1991, Rao et al., 1999, Gundling et al., 2010). This study demonstrated a stabilisation of pressures after 3 minutes, which would be preferable to patients over a longer familiarisation periods quoted in other studies.

The author acknowledges the limitation that there remains a slight, though non-significant decrease in resting pressure towards the end of the resting period and that this analysis period could have been extended to allow for further investigation of changes over time, however the average reduction in pressure over the last 2 minutes totalled only 2 mmHg. It seems unlikely that further extension of the familiarisation period would have clinical consequences significant enough to outweigh the merits of efficiency and participant comfort provided for by a shorter familiarisation period.

Analysis of repeat squeeze, endurance squeeze, demonstrated that there was no difference in results between repeated attempts. As a consequence, statistical analysis suggests that a reasonable protocol could include a single attempt at each manoeuvre. However the author acknowledges that it is likely that there will be a proportion of patients who have difficulty responding accurately to commands (for example in those with an element of dyssynergia) and for the purposes of uniformity a protocol with 2 of each test is suggested. An exception is proposed for endurance squeeze as this is an extension of 5-second squeeze and is a measure of fatigability. In those with poor anal function, it is likely that a repeat endurance squeeze would add significantly to results interpretation.

Interestingly analysis of push and cough demonstrated that although is no significant inter-individual variability on repeated manoeuvre attempts, and ICC statistics demonstrate generally good agreement, inspection of Bland-Altman plots suggested that there may be be potentially intra-individual variability on repeated manoeuvres which, although not statistically significant could be clinically relevant.

At present, the current convention is to report the results of both manoeuvres as single measurements from the anal canal, however these manoeuvres describe dynamic activity, which are particularly dependent on the volitional effort of the participant. It is conceivable that the intra-individual variability is in partially related to differences in this volitional effort. These data therefore raise the question as to whether an alternate method of analysis may be more appropriate (e.g. anal pressure changes relative to rectal pressure change or addition of qualitative descriptors).

The above point highlights a further possible limitation - that this protocol was developed in a healthy volunteer group. It is not inconceivable that alterations in anal function associated with pathology may result in differences of response to manoeuvres e.g. prolongation of time taken for recovery of baseline anal pressure during squeeze or cough. This is a limitation inherent during development of many novel techniques and interpretation of these findings should therefore be made with appropriate attention to the possible need for alteration following application to the patient population.

On the basis of these results the author proposes a standardised protocol illustrated in Figure 4-XI.

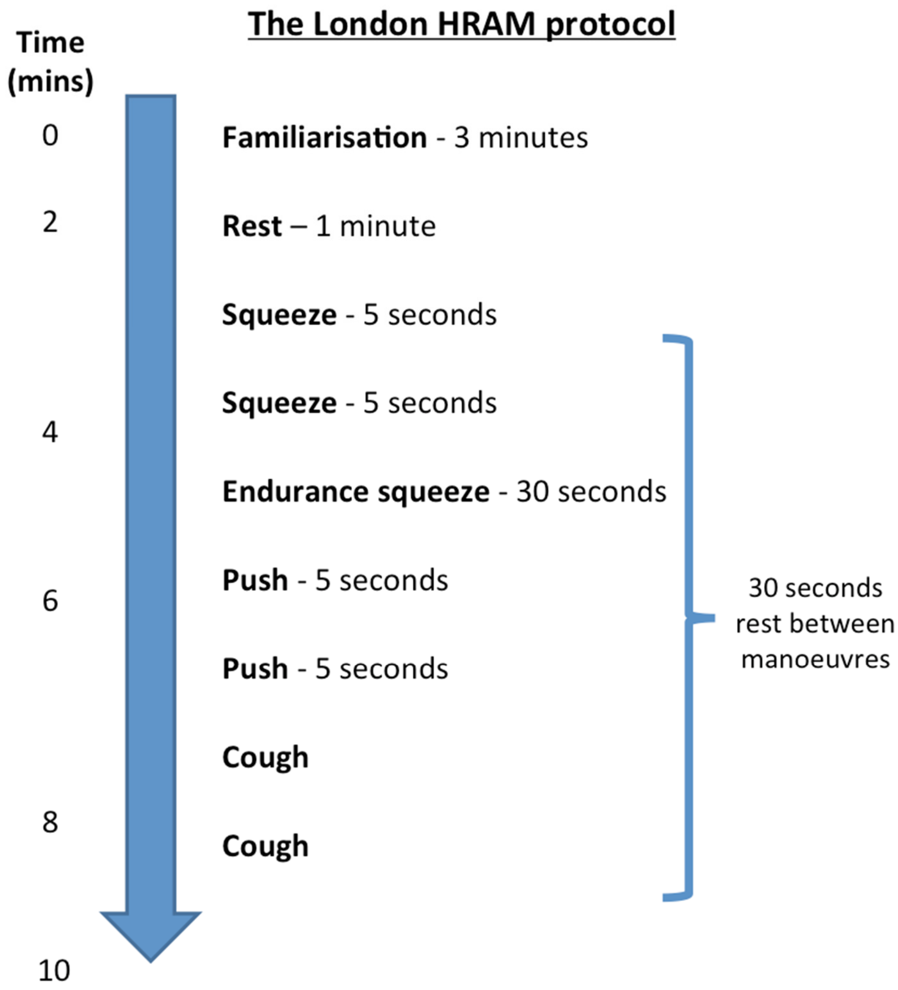

Figure 4-XI schematic of proposed standardised HRAM protocol.

All experiments in this chapter were performed by a single investigator (EVC) and there was no study of effects of encouragement on results of voluntary manoeuvres. On the basis of work by Heinrich *et al*. (Heinrich et al., 2013) the author accepts that there should be uniformity in the commands and encouragement given during the study protocol. This is a point that may be particularly pertinent during the comparison of results obtained by multiple practitioners from different institutions.

The development and validation of this standardised protocol was primarily to ensure uniformity of practices during subsequent data collection within this thesis, so that differences in results could be confidently attributed to patient / participant factors, rather than technical factors of data collection.

This study also fulfils a need within the literature and as a result of this work the protocol has been adopted as the agreed standard by the British Society of Gastroenterology (Association of GI Physiologists, 2013). Further acceptance and adoption of such a standardised protocol may be the first step towards discussion, collaboration and ultimately standardisation of HRAM practice between institutions.

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Chapter 5

5 Traditional measures of normal anorectal function using high-resolution anal manometry (HRAM) in 140 healthy volunteers

5.1 Rationale

Anorectal manometry is the most widely performed test for the assessment of anal sphincter function and anorectal co-ordination (Scott and Gladman, 2008). Nevertheless, previous chapters have demonstrated that both recording equipment and methodology remain unstandardized, which can significantly impact interpretation of results (Barnett et al., 1999, Rao et al., 2002).

The last decade has seen the development of high-resolution anal manometry (HRAM) with key improvements being: an increased number of closely spaced microtransducers greatly enhancing spatial resolution; the ability to measure pressure changes circumferentially; and software development to allow interpolation between adjacent microtransducers providing the operator with the option of detailed topographical plots of intraluminal pressure events relative to time and location; (Jones et al., 2007) data can be displayed as a colour contour plot, in contrast to a conventional line tracing.

Such technology has resulted in a paradigm shift in manometric testing of the upper gastrointestinal (GI) tract, with high-resolution oesophageal manometry now having replaced traditional manometry as the gold-standard investigation of oesophageal function (Bredenoord et al., 2012). However, despite recognised benefits there has been a slower implementation of high-resolution manometry for the assessment of anorectal function. Nevertheless the ability to visualize the anorectum as a dynamic structure during test manoeuvres should intuitively allow for a better appreciation of normal physiology and hopefully enhance our understanding of the pathophysiology of defaecatory dysfunction (Noelting et al., 2012, Ratuapli et al., 2012).

One of the principle challenges to adopting HRAM is to establish new normative data sets of an adequate size for recognized measures of anal sphincter function, and to promote standardisation of the technique so that results are transferrable between institutions; a problem that has bedevilled traditional practice (Rao et al., 2002). It is only following this that the impact of novel measures of anal function pertinent to this new technique can be properly developed, evaluated and implemented.

5.2 Aims

To date, there are only two published studies examining sphincter function in health using HRAM, both of which use the Manoview AR v1.0, Sierra Scientific Instruments system (Noelting et al., 2012, Li et al., 2013).

Given that equipment setup, catheter configuration and software analyses may affect results; the primary aim of this study was to provide a large dataset of parameters of normal anal sphincter function using an alternative, widely available HRAM system. The secondary aim was to qualitatively report phenomena noted during investigations that were previously difficult to recognize or overlooked using traditional manometry.

5.3 Methods

5.3.1 Subjects

Healthy, asymptomatic male and female subjects were recruited at Barts and the London School of Medicine and Dentistry, London. Ethical approval was granted by the Queen Mary University Research Ethics Committee (ref QMREC 2010/74 and QMREC 2013/12), and written informed consent obtained.

Recruitment method was identical to that utilised and outlined in Chapter 4.3.

In total 168 subjects were screened for eligibility. Of these 145 were recruited and 140 were enrolled in the study. A pictorial representation of this is seen in Figure 5-I below.

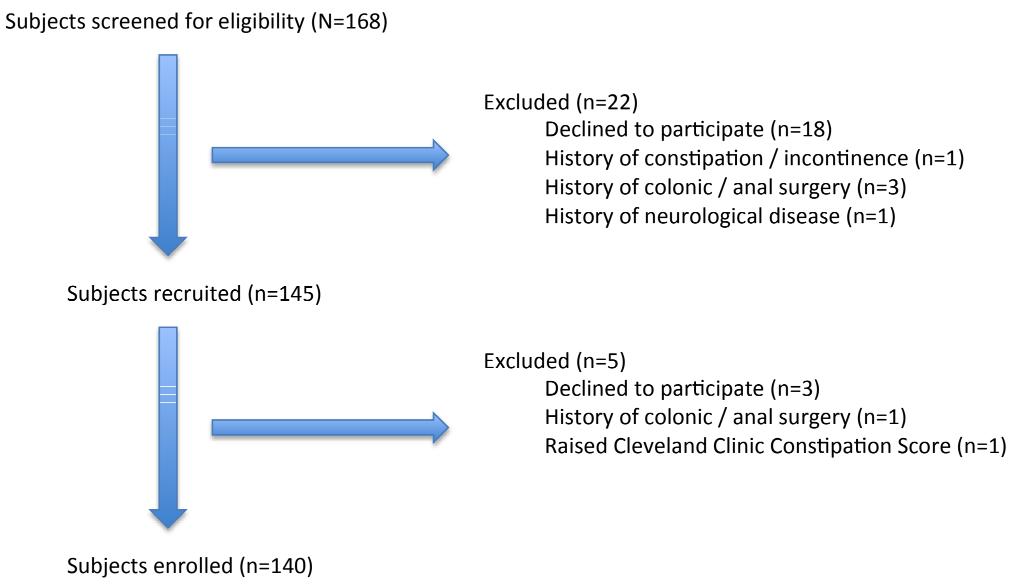

Figure 5-I Consort diagram illustrating study recruitment.

5.3.2 Equipment

HRAM was performed using a solid-state catheter (UniTip: UniSensor AG, Switzerland), of external diameter 12 F, incorporating 12 microtransducers, each of which measured pressure by means of a circumferential pressure sensor embedded within silicone gel. Ten of these sensors were spaced 0.8 cm apart, spanning 7.2 cm. The most proximal microtransducer was located within a non-latex balloon 3.3 cm proximal to these. The most distal sensor (located 2 cm below the most distal of the central 10 sensors) was used as an external reference.

Before every study, the catheter was immersed in tepid water for at least 3 minutes to pre-wet the sensors. Sensors were then zeroed to atmospheric pressure. Data acquisition, online visualization and signal processing were performed using a commercially available manometric system (Solar GI HRM v9.1, Medical Measurement Systems (MMS), Enschede, Netherlands).

5.3.3 Protocol

Each subject was instructed to defaecate if required prior to investigation. No bowel preparation given. All subjects were studied in the left-lateral position with knees and hips flexed. Prior to catheter insertion, a digital rectal examination was performed and the ability of the subject to understand the commands “squeeze” and “push” were confirmed.

All test manoeuvres were performed in accordance with published guidelines (Rao et al., 2002). The first 50 subjects underwent the extended protocol outlined in Chapter 4 of the thesis and the subsequent 90 underwent the standardised HRAM protocol developed following analysis Chapter 4 results. To perform the study, the catheter was inserted into the anorectum with the distal 2 microtransducers visible (the second most distal being located immediately outside of the anal verge). This is important, as if the second most distal sensor is inserted past the anal verge; interpolation of recorded pressures would provide an artificially elongated anal canal length.

Following a 3-minute run-in period for the purposes of familiarisation, manoeuvres were performed in a standard sequence with a 30 second recovery period between each manoeuvre (Figure 5-II):

Rest - Anorectal pressures were measured with the subject relaxed, lying still and not speaking for a period of 1 minute;

Squeeze - The subject was instructed to squeeze the anal canal as strongly possible for a period of 5 seconds;

Endurance squeeze - The subject was asked to squeeze the anal canal as strongly as possible for a period of 30 seconds;

Push (simulated defaecation)- Whilst still lying in the left lateral position, the subject was asked to bear down for 5 seconds as if to defecate;

Cough- The subject was asked to cough forcefully once on 2 occasions.

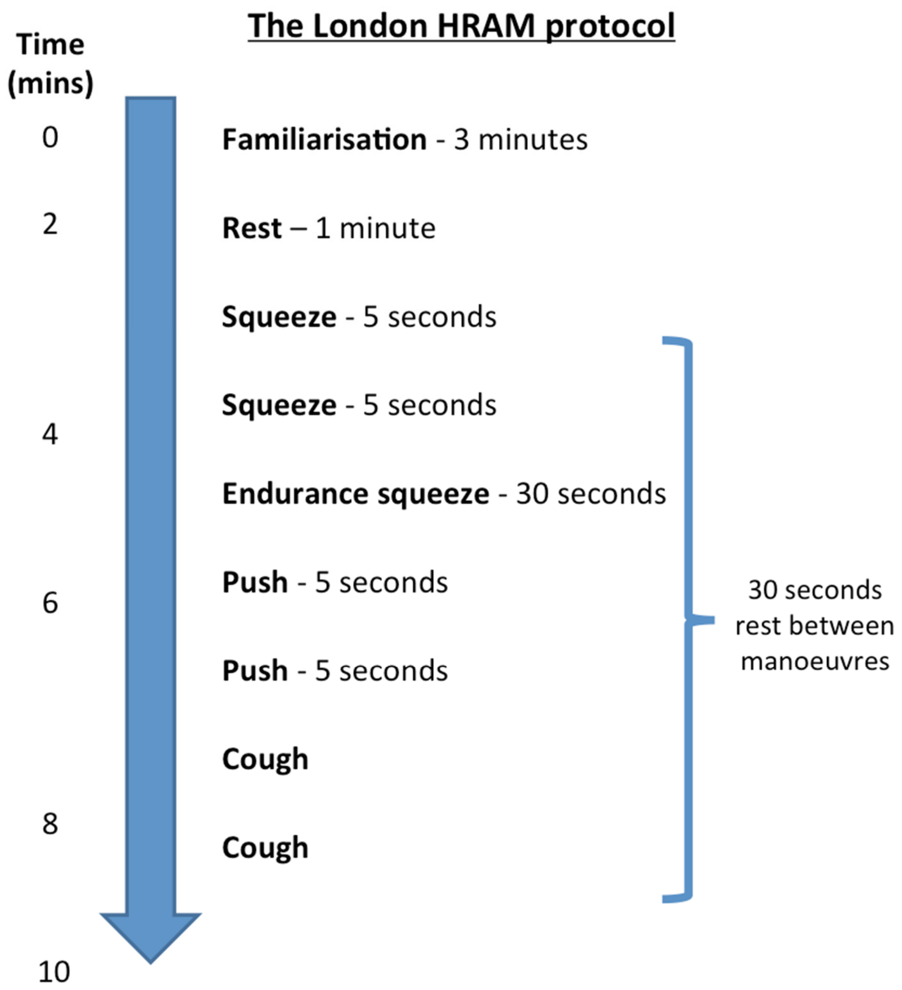

Figure 5-II Schematic of standardised HRAM protocol as developed in Chapter 4 of this thesis.

For squeeze, push and cough manoeuvres, the first attempt were used as practice, and the second attempt used for analysis. In the unusual event of poor participant compliance a further attempt was allowed at the practitioner's discretion.

5.3.4 Data analysis

For each manoeuvre period, the anal canal area was highlighted as an 'area of interest' using the e-sleeve box (Figure 5-II). This allowed the software to derive the maximum pressure recorded over this anal length at each point in time (sampling rate 10 Hz).

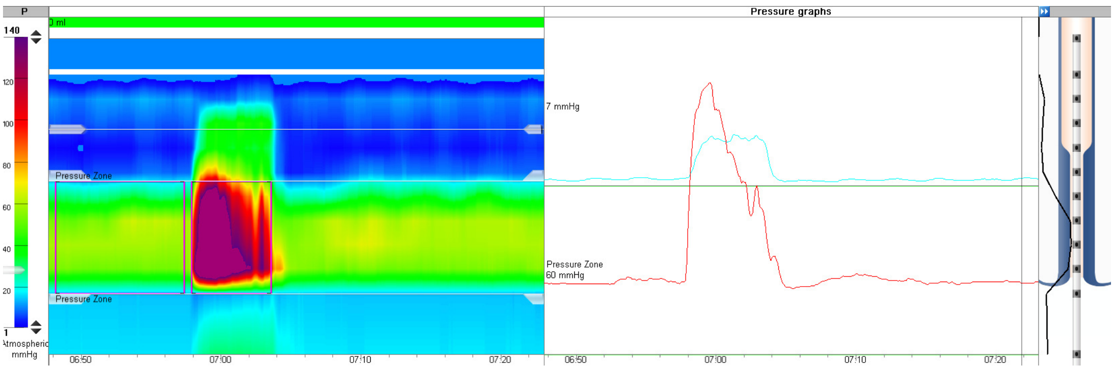

Figure 5-III Representative colour contour plot during a squeeze manoeuvre, demonstrating the use of the e-sleeve function. The left pane shows a colour contour data display with a pressure of 140 mmHg depicted purple and 0 mmHg as blue (pressure scale to the extreme left). The anal canal length is clearly displayed as a green band. During the squeeze manoeuvre the pressure within the anal canal increases, characterised by a change in the colour contour plot from green to purple.

On the right pane, the red manometric trace is derived from the maximum pressure within the anal canal e-sleeve ('area of interest' box overlying the distal and proximal borders of the anal canal length – within the colour contour plot). The light blue trace is representative of the rectal pressure at the point demonstrated in the left pane by the grey line.

Averages were then calculated automatically over the duration of the manoeuvre. The variables recorded together with their respective definitions are shown in Table 5-I.

Manoeuvre	Metric	Definition
Rest	Functional anal canal length	Length of anal canal (cm) in which pressure exceeds rectal pressure by >5 mmHg
	Average anal resting pressure	Average maximum pressure (mmHg) over the FACL during the 1 minute period of rest
Squeeze	Maximum absolute anal squeeze pressure	Highest recorded pressure (mmHg) at any point during the squeeze manoeuvre
	Maximum incremental anal squeeze pressure	Maximum recorded pressure (mmHg) at any point during voluntary squeeze, minus the mean maximum resting pressure prior to the manoeuvre (over 5 seconds)
	Average absolute anal squeeze pressure	Mean maximum recorded pressure (mmHg) over the duration of the 5 second voluntary squeeze manoeuvre
	Average incremental anal squeeze pressure	Mean maximum pressure (mmHg) sustained over the duration of the 5 second squeeze manoeuvre minus the mean maximum resting pressure prior to the manoeuvre (over 5 seconds)
Endurance squeeze	Endurance squeeze duration	Length in time (sec) over which a pressure at or above 50% of the highest recorded squeeze pressure is sustained. The endpoint is determined as the point at which the pressure first drops below this threshold
Push	Residual anal push pressure	Lowest maximum pressure (mmHg) recorded within the anal canal over the duration of the 5 second push manoeuvre
	Push relaxation percentage	Maximum relaxation percentage achieved over the duration of the 5-second push manoeuvre
	Push rectal peak pressure	Maximum pressure (mmHg) recorded from within the rectum over the duration of the 5-second push manoeuvre
	Rectoanal gradient	Difference between the push rectal peak pressure and the residual anal push pressure (mmHg)
Cough	Maximum absolute anal cough pressure	Highest recorded pressure within the anal canal (mmHg) at any point during the cough manoeuvre
	Maximum incremental anal cough pressure	Highest recorded pressure within the anal canal (mmHg) at any point during the cough manoeuvre, minus the maximum resting pressure prior to the manoeuvre (over 5 seconds)

Table 5-I Table of manoeuvre definitions and units of measurement.

5.3.5 Statistical analysis

Variables were summarised using number of observations, mean, standard deviation, median, minimum and maximum values. Reference ranges for manoeuvre variables were estimated directly from the 5th and 95th percentiles of the measurements. To assess the impact of age, sex and parity on these parameters (and thus the reporting strategy for normal ranges), initial Independent samples T tests were employed with further analysis using linear regression models as required. Statistical analyses were performed using a commercially available software package (SPSS Statistics Version 20: IBM, New York, USA). A P value of <0.05 was considered statistically significant.

5.4 Results

5.4.1 Subjects

A total of 140 volunteers were recruited for the study. All subjects tolerated the procedure without complication. Recruitment was weighted towards parous females, as this is representative of the patient cohort that usually present for assessment of anal sphincter function (Pretlove et al., 2006, Whitehead et al., 2009a).

Age demographics for the group are shown below in Table 5-II. Participant age were normally distributed for both the male (mean age 41 ± 15 years, Z scores = 1.44 skewness, = 1.33 kurtosis) and female groups (mean age 42.4 ± 12.7 years, Z scores = .21 skewness, = 2.16 kurtosis). There was no difference in age between the male and female groups overall (95% CI, -4.36 to 7.12), $t(49) = .482$, Independent sample T test $p = .632$.

Descriptives

	N	Mean	SD	Median	Min	Max
Females	106	42.4	12.7	44	18	68
Nulliparous	42	35.8	13.1	33	18	68
Parous	64	46.8	10.5	47	25	68
Males	34	41	15	37	21	71

Table 5-II Table of age descriptives subdivided by sex and parity.

When the female group was subdivided into parous and nulliparous females, these groups remained normally distributed for age (parous Z scores = .52 skewness, = 1.39 kurtosis; nulliparous Z scores = 2.34 skewness, = .164 kurtosis). The parous group were significantly older than the nulliparous group: parous mean age 46.8 ± 10.4 years *vs.* nulliparous females mean age 35.7 ± 13.1 years (95% CI, -15.8 to -6.2), $t(74) = -4.259$, Independent sample T test $p < .0001$.

Within the parous group (N=64), 17 had more than two vaginal deliveries, 3 had two or more deliveries requiring instrumental assistance, 6 had two or more deliveries associated with episiotomy and 4 had two or more deliveries associated with a perineal tear (Table 5-III.)

Frequencies

	Pregnancies		Vaginal deliveries		Instrumental deliveries		Episiotomies		Perineal tears	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
0	n/a	n/a	8	12.5	49	76.6	42	65.6	39	60.9
1	22	34.4	22	34.4	12	18.8	16	25	21	32.8
2	35	39.1	17	26.2	2	3.1	6	9.4	3	4.7
3	20	15.6	10	15.6	1	1.6	0	0	0	0
4	4	6.3	4	6.3	0	0	0	0	1	1.6
5	3	4.7	3	4.7	0	0	0	0	0	0
TOTAL	64	100	64	100	64	100	64	100	64	100

n/a = not applicable

Table 5-III Table of obstetric events in parous females.

Quantitative values for each manoeuvre are shown below: all females (Table 5-IV), nulliparous females (Table 5-V), parous females (Table 5-VI) and males (Table 5-VII).

Descriptive statistics - All females

		N	Mean	SD	Median	Min	Max
Rest	Functional anal canal length (cm)	106	3.5	0.82	3.4	6	4.4
	Average anal resting pressure (mmHg)	106	64	18	63	25	111
Squeeze	Maximum absolute anal squeeze pressure (mmHg)	106	229	90	231	76	503
	Maximum incremental anal squeeze pressure (mmHg)	106	168	83	164	27	429
	Average absolute anal squeeze pressure (mmHg)	106	177	72	171	24	387
	Average incremental anal squeeze pressure (mmHg)	106	117	64	107	20	281
Endurance squeeze	Endurance squeeze duration (seconds)	106	11	9.5	6	2	30
Push	Residual push pressure (mmHg)	106	45	21	42	12	110
	Push relaxation percentage (% pre manoeuvre pressure)	106	24	22	22	0[a]	83
	Peak rectal push pressure (mmHg)	106	62	31	55	18	200
	Rectoanal gradient (mmHg)	106	16	35	14	-88	142
Cough	Maximum absolute anal cough pressure (mmHg)	106	175	69	164	58	460
	Maximum incremental anal cough pressure (mmHg)	106	115	66	103	7	408

(a) Substitute value of 0 as lowest relaxation percentage was negative i.e. representing a paradoxical anal contraction during push

Table 5-IV Table of summary statistics for traditional measures of anorectal function using HRAM in all females.

Descriptive statistics - Nulliparous females

		N	Mean	SD	Median	Min	Max
Rest	Functional anal canal length (cm)	42	3.5	0.95	3.5	2	6
	Average anal resting pressure (mmHg)	42	66	17	62	44	111
Squeeze	Maximum absolute anal squeeze pressure (mmHg)	42	266	97	267	81	503
	Maximum incremental anal squeeze pressure (mmHg)	42	200	89	189	43	429
	Average absolute anal squeeze pressure (mmHg)	42	209	76	209	63	387
	Average incremental anal squeeze pressure (mmHg)	42	144	68	135	29	281
Endurance squeeze	Endurance squeeze duration (seconds)	42	12	10.2	8	2	30
Push	Residual push pressure (mmHg)	42	45	18	42	13	87
	Push relaxation percentage (% pre manoeuvre pressure)	42	26	23	23	0[a]	83
	Peak rectal push pressure (mmHg)	42	62	46	53	18	200
	Rectoanal gradient (mmHg)	42	17	35	7	-37	142
Cough	Maximum absolute anal cough pressure (mmHg)	42	189	65	180	82	316
	Maximum incremental anal cough pressure (mmHg)	42	127	62	112	32	253

(a) Substitute value of 0 as lowest relaxation percentage was negative i.e. representing a paradoxical anal contraction during push

Table 5-V Table of summary statistics for traditional measures of anorectal function using HRAM in nulliparous females.

Descriptive statistics - Parous females

		N	Mean	SD	Median	Min	Max
Rest	Functional anal canal length (cm)	64	3.4	0.7	3.4	1.6	5.2
	Average anal resting pressure (mmHg)	64	63	19	63	25	107
Squeeze	Maximum absolute anal squeeze pressure (mmHg)	64	204	77	196	76	393
	Maximum incremental anal squeeze pressure (mmHg)	64	146	72	141	27	323
	Average absolute anal squeeze pressure (mmHg)	64	156	61	151	24	337
	Average incremental anal squeeze pressure (mmHg)	64	99	54	92	20	76
Endurance squeeze	Endurance squeeze duration (seconds)	64	10	9	6	2	30
Push	Residual push pressure (mmHg)	64	45	22	42	12	110
	Push relaxation percentage (% pre manoeuvre pressure)	64	22	21	22	0[a]	68
	Peak rectal push pressure (mmHg)	64	61	27	56	21	140
	Rectoanal gradient (mmHg)	64	16	35	17	-88	102
Cough	Maximum absolute anal cough pressure (mmHg)	64	166	69	156	58	460
	Maximum incremental anal cough pressure (mmHg)	64	107	67	90	7	408

(a) Substitute value of 0 as lowest relaxation percentage was negative i.e. representing a paradoxical anal contraction during push

Table 5-VI Table of summary statistics for traditional measures of anorectal function using HRAM in parous females.

Descriptive statistics - Males

		N	Mean	SD	Median	Min	Max
Rest	Functional anal canal length (cm)	34	4.3	1	4.5	2.3	6.5
	Average anal resting pressure (mmHg)	34	75	21	72	38	136
Squeeze	Maximum absolute anal squeeze pressure (mmHg)	34	315	143	275	94	732
	Maximum incremental anal squeeze pressure (mmHg)	34	240	137	215	61	643
	Average absolute anal squeeze pressure (mmHg)	34	228	107	205	86	563
	Average incremental anal squeeze pressure (mmHg)	34	153	101	136	40	474
Endurance squeeze	Endurance squeeze duration (seconds)	34	15	11.8	18	1	30
Push	Residual push pressure (mmHg)	34	64	22	66	20	105
	Push relaxation percentage (% pre manoeuvre pressure)	34	13	28	14	0[a]	60
	Peak rectal push pressure (mmHg)	34	76	43	76	13	209
	Rectoanal gradient (mmHg)	34	14	35	9	-44	133
Cough	Maximum absolute anal cough pressure (mmHg)	34	243	117	217	75	516
	Maximum incremental anal cough pressure (mmHg)	34	168	113	140	16	434

(a) Substitute value of 0 as lowest relaxation percentage was negative i.e. representing a paradoxical anal contraction during push

Table 5-VII Table of summary statistics for traditional measures of anorectal function using HRAM in males.

5.4.2 Independent samples t-test – effect of sex on traditional measures of anal function

Though the primary aim of this observational study in health was not to sub-analyse normative data on the bases of demographics, traditional anal manometry is conventionally approached from the perspective that males and females differ and that within women, age and parity have an effect on anal sphincter function (Poos et al., 1986, McHugh and Diamant, 1987, Pedersen and Christiansen, 1989, Ryhammer et al., 1997). Thus, secondary analyses were performed to study the influence of these possible explanatory variables on the cohort as a whole.

Visualisation of Q-Q / stem and leaf plots demonstrated that male and female data for all measures was broadly normally distributed allowing the application of parametric statistical tests. Initial group comparisons between males and females were performed using the independent samples T test, the results of which are summarised in Table 5-VIII

Similar to previous studies (Akervall et al., 1990, Gundling et al., 2010) there appeared to be significant differences in anal function between men and women. With regards to the resting manoeuvre, men displayed significantly higher mean anal resting pressures (75.2 ± 21 mmHg *vs.* 64.2 ± 18.5 mmHg [95% CI, -19.1 to -2.91], $t[50] = -2.730$, $p = .009$) and significantly longer anal canal lengths (4.3 ± 1.0 cm *vs.* 3.5 ± .82 cm [95% CI, -1.23 to -.44], $t[47] = -4.272$, $p < .0005$) than women.

Group Statistics and Independent samples test

		Sex	Mean	SD	Sig
Rest	Anal canal length (cm)	F	3.46	0.82	***
		M	4.29	1.04	
	Mean anal resting pressure (mmHg)	F	64.2	18.5	**
		M	75.2	21.0	
Squeeze	Maximum absolute squeeze pressure (mmHg)	F	228.9	90.4	**
		M	315.1	143.3	
	Maximum incremental squeeze pressure (mmHg)	F	167.8	83.2	**
		M	240.4	137.1	
	Mean absolute squeeze pressure (mmHg)	F	176.8	71.9	*
		M	228.0	107.1	
	Mean incremental squeeze pressure (mmHg)	F	116.8	63.9	0.053
		M	153.4	100.9	
Endurance squeeze	Endurance squeeze duration (secs)	F	11.1	9.5	0.076
		M	15.2	11.8	
Push	Push residual pressure (mmHg)	F	45.4	20.6	***
		M	63.6	21.9	
	Push relaxation percentage (% pre manoeuvre baseline)	F	23.8	22.2	*
		M	13.1	27.9	
	Push rectal peak pressure (mmHg)	F	61.6	31.2	0.051
		M	77.5	42.8	
	Rectoanal gradient (mmHg)	F	16.2	35.1	0.746
		M	14.0	35.6	
Cough	Maximum anal cough pressure (mmHg)	F	175.2	68.6	**
		M	243.3	116.6	
	Maximum incremental anal cough pressure (mmHg)	F	114.9	65.6	*
		M	168.4	113.4	

* Statistically significant at the $p< .05$, ** $p< .01$ level, *** $p< .001$ level (2-tailed)

M = males, F = females

Table 5-VIII Summary table of group statistics for traditional measures of anorectal function as measured by HRAM in males (N=34) and females (N=106). Males are characterised as having generally higher pressures during the rest, squeeze and cough manoeuvres.

During the squeeze manoeuvre, there were also differences between the male and female groups, with men generating higher anal pressure as measured by the maximum absolute squeeze pressure (315.1 ± 143.3 mmHg *vs.* 228.9 ± 90.4 mmHg [95% CI, -138.9 to -33.53], $t[42] = -3.31$, $p = .002$), maximum incremental squeeze pressure (240.4 ± 137.1 mmHg *vs.* 167.7 ± 83.2 mmHg [95% CI, -122.9 to -22.5], $t[41] = -2.923$, $p = .006$) and mean absolute squeeze pressure (228.1 ± 107.2 mmHg *vs.* 176.8 ± 71.8 mmHg [95% CI, -90.9 to –11.64], $t[43] = -2.609$, $p = .012$) than females. However, difference between groups for the most conservative of the squeeze measures, the mean incremental squeeze pressure was marginally not significant (153.44 ± 100.9 mmHg in males *vs.* 116.8 ± 63.8 mmHg in females [95% CI, -73.7 to .486], $t[42] = -1.992$, $p = .053$).

With regards to push, females better displayed the ability to relax the anal canal during the manoeuvre. There was not only a significantly reduced push residual pressure in the female group when compared to males, (45.46 ± 20.6 mmHg in females *vs.* 63.6 ± 21.9 mmHg in males respectively [95% CI, -26.7 to –9.7], $t[53] = -4.279$, $p < .0005$), but also a greater percentage relaxation (23.8 ± 22.1 mmHg in females *vs.* 13.1 ± 27.8 mmHg in males [95% CI, .231 to 21.31], $t[43] = -2.007$, $p = .045$) suggesting a more optimal pattern of defaecation in females.

5.4.3 Hierarchical multiple regression – modelling of age and sex on traditional measures of anal function

To further examine the effects of age and sex on anal function in health, a hierarchical multiple regression model was built to evaluate the association between these factors on average anal resting pressure and average incremental anal squeeze pressure as measured by HRAM.

A two-stage hierarchical regression construct was built, with the average anal resting pressure and average incremental anal squeeze pressure as the dependent variables, in two separate models.

In step 1 of the regression; participant sex (dummy coded: female 0, male 1) was proposed as the first independent variable. In step 2, age was posited as another independent variable, to examine the unique contribution of age in predicting each measure, over and above the contribution of sex in step 1.

For evaluation of pressures during rest, step 1 of the model demonstrated that male sex predicted higher anal resting pressures, with this factor explaining 5.1% of the variability in end resting scores (F(1, 138) = 8.503, p = .004. The addition of age as a separate independent variable did not add significantly to the model (R^2 change of .001, F[1, 137] = .125, p = .725), suggesting that age was not predictive of resting pressures. However, the full model of sex and age to predict average anal resting pressure was statistically significant, R^2 = .059, F(2, 137) = 4.287, p = .016; adjusted R^2 = .045.

Hierarchical regression

Dependent variables		Step 1				Step 2				
		Sex (β)	R^2	Adj. -R^2	F-ratio	Age (β)	R^2	Adj. -R^2	R^2 Change	F-ratio
Model 1	Mean anal resting pressure (mmHg)	.241** (2.91)	0.058	.045	8.503 **	-.029 (-.353)	.059	.045	.001	4.287 *
Model 2	Mean incremental squeeze pressure (mmHg)	.208* (2.497)	.043	.306	6.234 *	-.176* (-2.14)	.074	.061	.031	5.496 **

* Statistically significant at the p< .05, ** p< .01 level (2-tailed)

Table 5-IX Table of standardised regression coefficients evaluating the association between sex and age on anal resting and squeeze pressures. Data pertains to male (N=34) and female (N=106) healthy volunteers.

Similarly, for evaluation of pressures during the squeeze manoeuvre, step 1 of the model once more demonstrated that male sex predicted higher mean incremental squeeze pressures than females with sex explaining 3.6% of the variability in end scores (F(1, 138) = 6.234, p = .014. In this model, the addition of age as a separate independent variable did add significantly to the model, with age predicting marginally lower scores (-1 mmHg per increasing year of age), (R^2 change of .031, F(1, 137) = 4.597, p = .034). Once more, the full model of sex and age to predict mean incremental squeeze pressure was statistically significant, R^2 = .061, F(2, 137) = 5.496, p = .005; adjusted R^2 = .061.

Table 5-IX displays the standardized regression coefficients (β), the *t*-values, R^2 and adjusted R^2 for step 1 (sex) and step 2 (age) for both the resting and squeeze models.

5.4.4 Independent samples t-test – effect of age and parity on traditional measures of anal function in healthy females

Similar to the data for males and females, visualisation of Q-Q / stem and leaf plots demonstrated that data for all measures in parous and nulliparous females were broadly normally distributed allowing the application of parametric statistical tests. Initial group comparisons between nulliparous and parous females were performed using the independent samples T test, the results of which are summarised in Table 5-X.

Similar to previous studies, group comparisons demonstrated a significant decrease in all measures of squeeze function associated with parity. Most notably, there was a highly significant difference in the most conservative measure, mean incremental squeeze pressure (144.0 ± 68.1 mmHg in nulliparous *vs.* 98.9 ± 54.3 mmHg in parous females respectively [95% CI, 20.1 to 70.0], $t[74] = 3.597$, $p = .001$) with parous females generating scores on average 45.1mmHg lower than nulliparous females.

The effect of increasing multiparity was also analysed using a one way between subjects ANOVA to assess if mean incremental squeeze pressure decreased significantly with increasing number of previous pregnancies. This analysis demonstrated that there was no significant effect of number of pregnancies ($F\,(4, 59) = 0.639$, $p = .644$).

There was no significant difference in measures of anal pressure during rest, endurance squeeze, push or cough between the nulliparous and parous groups.

Group Statistics and Independent samples test

		Parity	Mean	SD	Sig
Rest	Anal canal length (cm)	N	3.54	0.94	0.403
		P	3.40	0.73	
	Mean anal resting pressure (mmHg)	N	66.3	17.1	0.317
		P	62.7	19.3	
Squeeze	Maximum absolute squeeze pressure (mmHg)	N	266.4	97.3	**
		P	204.3	76.9	
	Maximum incremental squeeze pressure (mmHg)	N	200.7	88.9	**
		P	146.1	72.1	
	Mean absolute squeeze pressure (mmHg)	N	209.0	75.7	***
		P	155.6	61.1	
	Mean incremental squeeze pressure (mmHg)	N	144.0	68.2	**
		P	99.0	54.4	
Endurance squeeze	Endurance squeeze duration (secs)	N	12.6	10.2	0.213
		P	10.1	9.0	
Push	Push residual pressure (mmHg)	N	45.2	17.9	0.944
		P	45.5	22.3	
	Push relaxation percentage (% pre manoeuvre baseline)	N	26.3	23.3	0.374
		P	22.3	21.4	
	Push rectal peak pressure (mmHg)	N	61.8	36.4	0.959
		P	61.5	27.6	
	Rectoanal gradient (mmHg)	N	16.6	35.4	0.93
		P	16.0	35.1	
Cough	Maximum anal cough pressure (mmHg)	N	189.1	65.4	0.086
		P	166.0	69.6	
	Maximum incremental anal cough pressure (mmHg)	N	127.0	61.5	0.117
		P	106.9	67.4	

* Statistically significant at the *p*< .05, ** *p*< .01 level, *** *p*< .001 level (2-tailed)

N = nulliparous, P = parous

Table 5-X Summary table of group statistics for traditional measures of anorectal function as measured by HRAM in nulliparous (N=42) and parous (N=64) females. Nulliparous females display globally higher anal squeeze pressures.

5.4.5 Hierarchical multiple regression – modelling of parity and age on parameters of anal squeeze function

As demographic analyses in Chapter 5.4.1 demonstrated significant differences in age between parous and nulliparous females, in a similar fashion to Chapter 5.4.3, a hierarchical multiple regression model was built to evaluate the predictive ability of age and parity on mean incremental squeeze pressure in the female cohort.

A two-stage hierarchical regression construct was built with average incremental anal squeeze pressure as the dependent variable. In step 1 of the regression; participant parity (dummy coded: nulliparous 0, parous 1) was proposed as the independent variable. In step 2, age was posited as another independent variable to examine its unique contribution over and above the contribution of parity in step 1.

Step 1 of the model demonstrated that parity predicted lower mean incremental squeeze pressures explaining 3.6% of the variability in end scores (F(1, 138) = 6.233, p = .014. The addition of age as a separate independent variable added significantly to the model, R^2 change of .034, F(1, 137) = 4.597, p = .034, suggesting that age was also predictive of mean incremental squeeze pressures. The full model of parity and age to predict mean incremental squeeze pressures was statistically significant, R^2 = .074, F(2, 137) = 5.496, p = .005; adjusted R^2 = .074.

Table 5-XI displays the standardized regression coefficients (β), the t-values, R^2 and adjusted R^2 for step 1 (parity) and step 2 (age) for the model.

Hierarchical regression

Dependent variable		Step 1				Step 2				
		Parity (β)	R^2	Adj.-R^2	F-ratio	Age (β)	R^2	Adj.-R^2	R^2 Change	F-ratio
Model 1	Mean incremental squeeze pressure (mmHg)	.208* (2.49)	0.043	.036	6.233 *	-.176 (-2.14)	.074	.061	.031	5.496 **

* Statistically significant at the *p*< .05, ** *p*< .01 level (2-tailed)

Table 5-XI Table of standardised regression coefficients evaluating the association between parity and age mean anal s. Data pertains to nulliparous (N=42) and parous (N=62) female healthy volunteers.

5.4.6 Interim conclusions

As regression modelling in Chapters 5.4.3 and 5.4.5 demonstrate a marginal effect of age on parameters of anal function, subsequent data for the assessment of normal values have been presented on the basis of gender and parity without consideration of age.

5.4.7 Normal values for use in clinical practice

Due to significant variability between groups suggested normal ranges have been based on 5th and 95th percentiles rather than confidence intervals and are outlined below in Table 5-XII.

Normal values

		all females		parous females		nulliparous females		males	
		lower	upper	lower	upper	lower	upper	lower	upper
Rest	Functional anal canal length (cm)	2.3	5	2.3	4.9	2.1	5	2.4	6.1
	Average anal resting pressure (mmHg)	33	100	32	100	46	108	45	123
Squeeze	Maximum absolute anal squeeze pressure (mmHg)	91	392	88	377	91	471	108	626
	Maximum incremental anal squeeze pressure (mmHg)	45	320	44	307	47	380	62	555
	Average absolute anal squeeze pressure (mmHg)	74	309	71	301	78	334	91	465
	Average incremental anal squeeze pressure (mmHg)	29	234	25	220	34	266	47	393
Endurance squeeze	Endurance squeeze duration (seconds)	2	30	3	30	2	30	2	30
Push	Residual push pressure (mmHg)	16	84	15	98	17	75	22	104
	Push relaxation percentage (% pre push pressure)	0[a]	66	0[a]	65	0[a]	78	0[a]	53
	Peak rectal push pressure (mmHg)	21	119	22	126	20	120	18	172
	Rectoanal gradient (mmHg)	-34	91	36	88	-24	99	-40	100
Cough	Maximum absolute anal cough pressure (mmHg)	82	300	71	292	92	314	99	503
	Maximum incremental anal cough pressure (mmHg)	34	225	292	34	221	240	36	418

(a) Substitute value of 0 as lowest relaxation percentage was negative i.e. representing a paradoxical anal contraction during push

Table 5-XII Table of suggested normal values for traditional measures of anorectal function as determined by HRAM. Limits based on 5th and 95th percentiles.

5.4.8 Qualitative colour contour plot findings

5.4.8.1 Rest

Data displays with the colour contour plots allowed clear appreciation of varying pressures within the anal canal (Figure 5-IV).

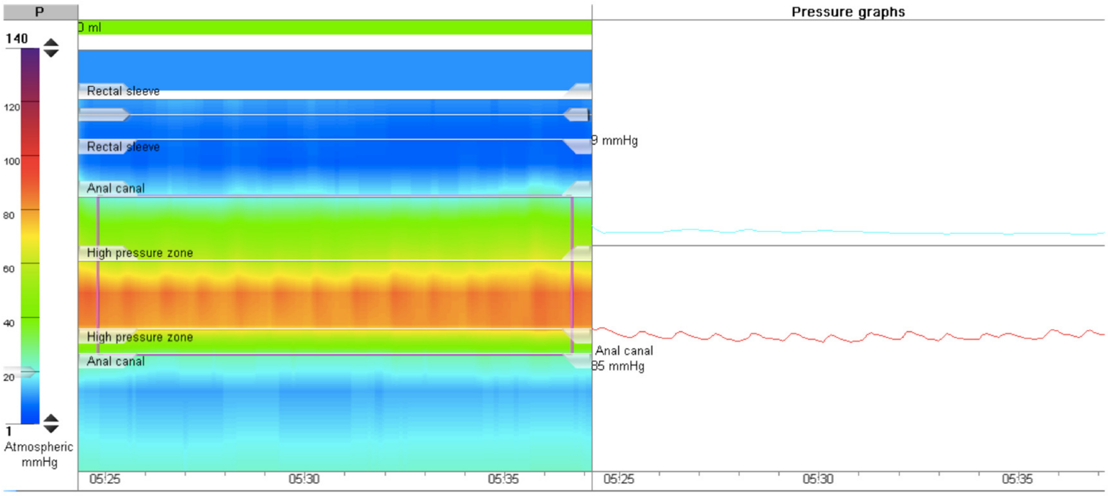

Figure 5-IV Representative colour contour plot and corresponding line trace (rectal pressure in blue above, anal pressure in red below) from a volunteer during the resting manoeuvre. Anal pressures within the high pressure zone (seen as a band of red overlying the green demarcation of the anal canal) are seen to fluctuate in a sinusoidal fashion (seen on the lower pressure trace in red).

In the majority of subjects, an intra-anal high-pressure zone was appreciated. In a proportion of subjects, slow pressure waves were recorded at a frequency of 9 – 19 cycles/minute, and were seen to be superimposed on the basal resting pressure. Also, in a further subgroup, more dramatic ultra-slow pressure waves, at a frequency of 1 – 2 cycles/minute were observed (Figure 5-V).

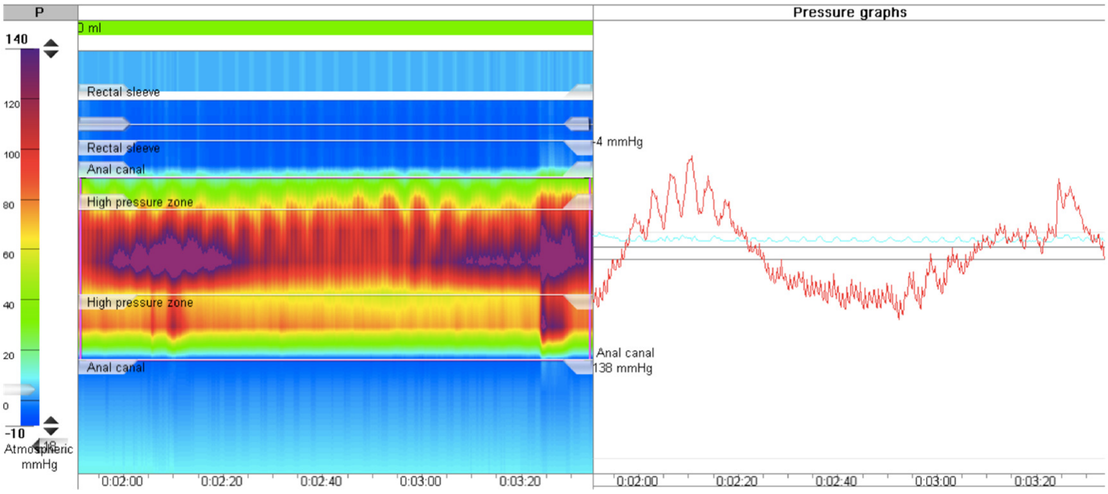

Figure 5-V Representative colour contour plot and corresponding line trace (rectal pressure in blue above, anal pressure in red below) from a volunteer during the resting manoeuvre. Anal pressures within the high-pressure zone are exhibiting characteristic ultra-slow pressure waves, seen as patches of purple superimposed over the yellow/green anal canal.

5.4.8.2 Squeeze

Inspection of squeeze morphology using the colour contour plots revealed heterogeneity of squeeze pattern between individuals. Contribution to squeeze did not necessarily involve the whole anal canal.

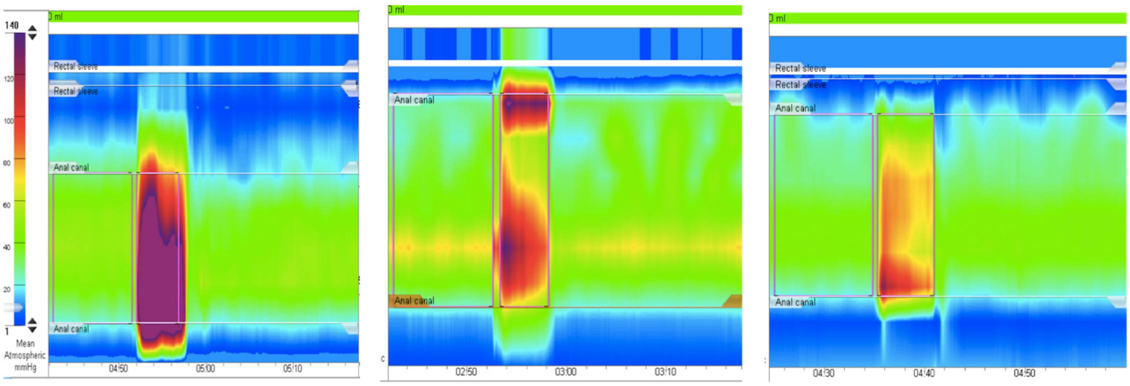

Figure 5-VI Representative colour contour plots from 3 individuals during the squeeze manoeuvre. Each squeeze was reported similarly i.e. maximum squeeze pressure ~160mmHg. Close inspection of the morphology of sphincteric response to squeeze however demonstrates potentially significant differences between individuals.

Squeeze (a) involves the whole anal sphincter, squeeze (b) shows a significant contribution from puborectalis and squeeze (c) reveals that the majority of force is generated by the distal sphincter. In some, contribution by (presumed) puborectalis appeared predominant; in others, squeeze appeared mainly as a result of contraction of the distal portion of the anal sphincter (Figure 5-VI). Due to the use of the e-sleeve function (that records only the maximum pressure within the selected area at each point in time) these differences were not highlighted quantitatively.

5.4.8.3 Push

The use of the colour contour plots clearly highlighted co-ordinated recto-anal events during the push manoeuvre (Figure V-II).

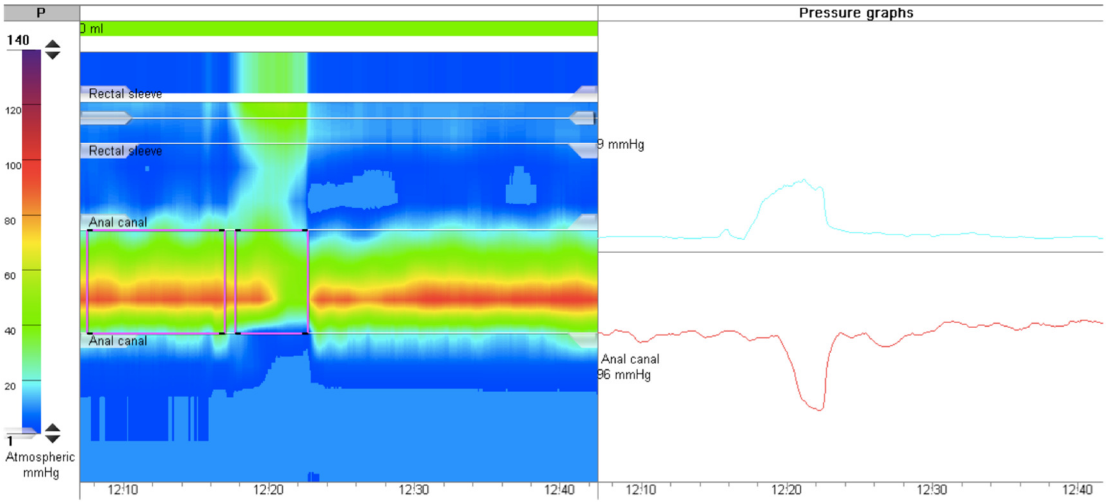

Figure 5-VII Representative colour contour plot and corresponding line trace (rectal pressure in blue above, anal pressure in red below) from a volunteer during a push. Anal pressures are seen to drop and rectal pressures are seen to rise during the manoeuvre.

Qualitative interpretation of anal pressures relative to rectal pressures was aided by the ability to use the colour display to show either 'absolute' or 'relative to rectal' pressures (Figure 5-VIIII).

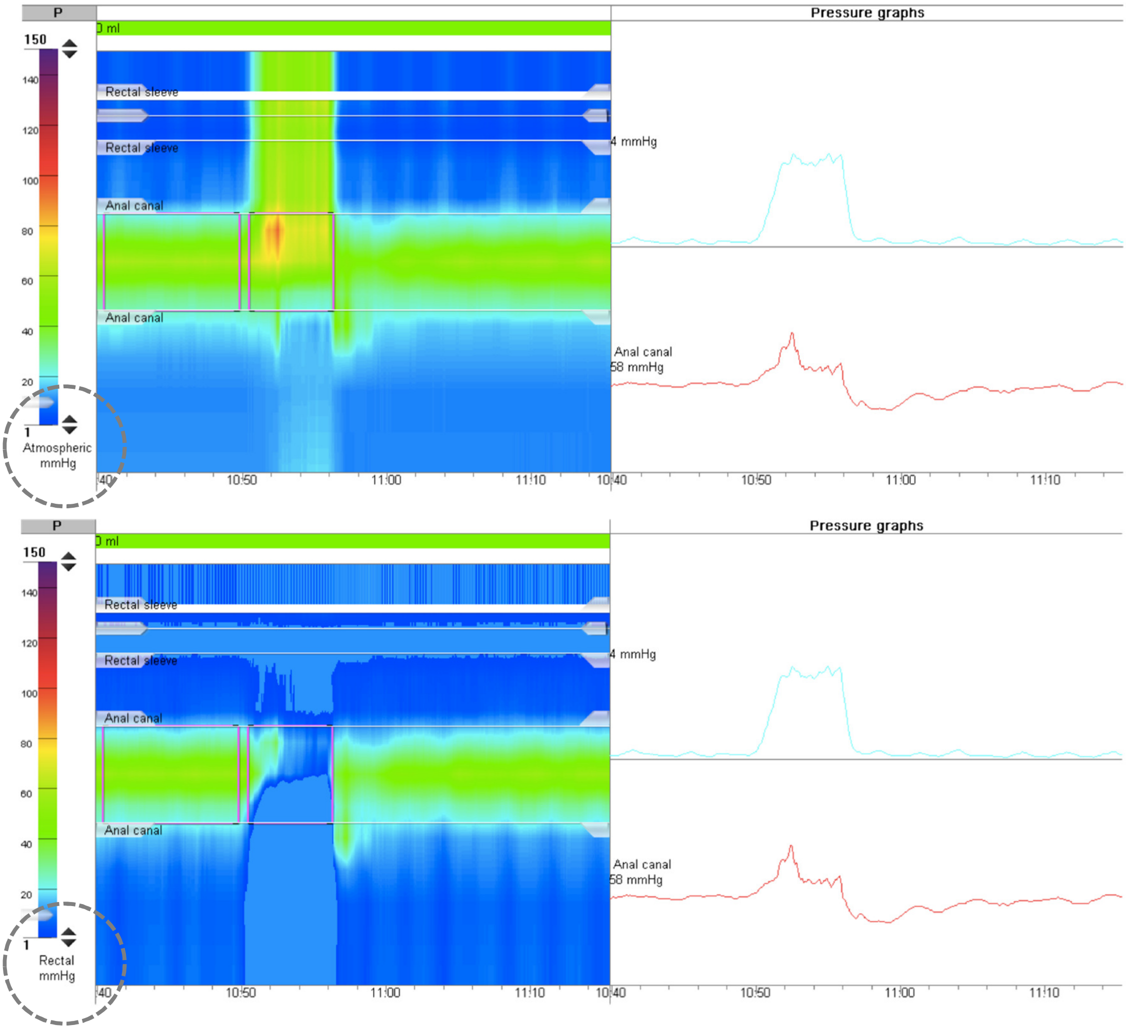

Figure 5-VIII Two representative colour contour plots and corresponding line traces (rectal pressure in blue above, anal pressure in red below) of the same push manoeuvre. Colours in the plot above are referenced to atmospheric pressure. Inspection of this plot demonstrates an increase in upper anal canal pressure, a finding which may be considered dyssynergic. Alteration of the colour scale to a rectal reference (lower plot) demonstrates that during the push manoeuvre, anal pressures drop markedly relative to rectal pressure, suggesting a normal pattern of push.

As previously demonstrated, there was failure of some healthy volunteers to increase the rectoanal gradient during push; however, in some, a delayed relaxation of the anal canal was seen which could be considered a normal variant (Figure 5-XI).

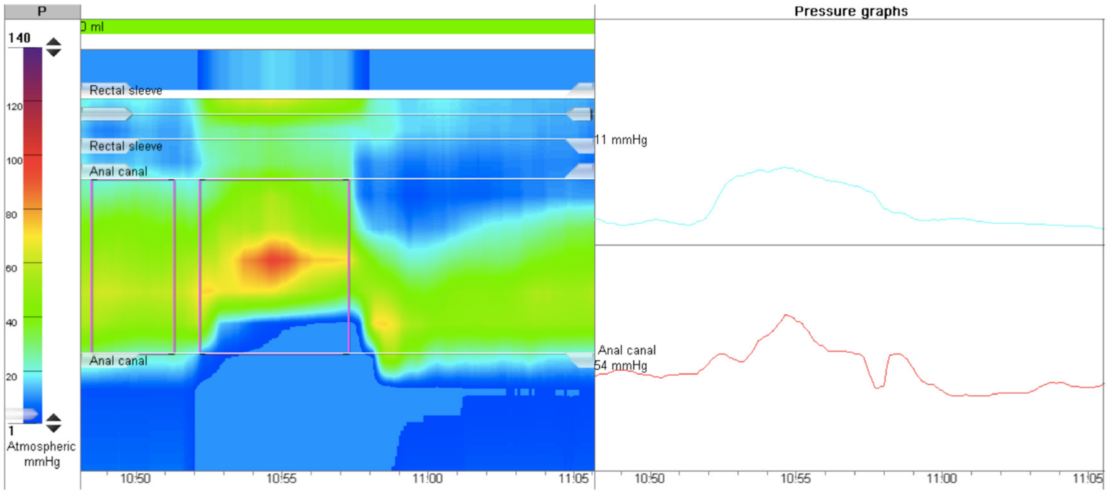

Figure 5-IX Representative colour contour plot and corresponding line trace (rectal pressure in blue above, anal pressure in red below) of a push. During the manoeuvre, rectal pressures are seen to rise. During this time, anal pressures are also seen to rise (which may be considered an abnormal response). Following the end of the manoeuvre upper anal canal pressures drop below baseline. This delayed anal relaxation during push may be considered a normal variant.

5.4.8.4 Cough

Qualitative inspection of cough manoeuvres clearly demonstrated the anal response to cough (Figure 5-X).

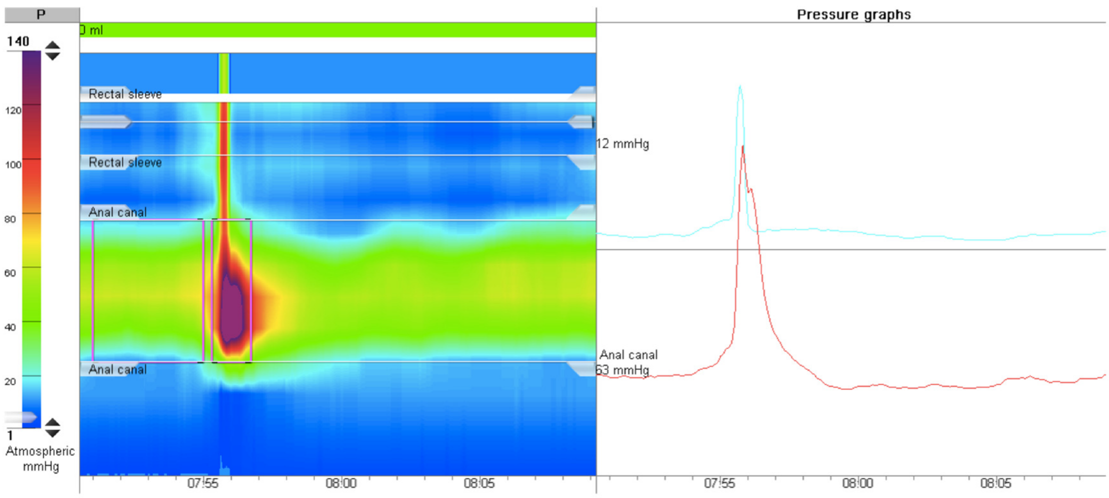

Figure 5-X Representative colour contour plot and corresponding line trace (rectal pressure in blue above, anal pressure in red below) of anorectal response to a cough. During the manoeuvre anal pressures are seen to rise above rectal pressure. In addition the anal response time appears longer than the rectal response time.

In all volunteers, pressures within the anal canal exceeded rectal pressures during this manoeuvre. However, some volunteers appeared to exhibit a post cough relaxation of the upper segment of the anal canal (Figure 5-XI), a finding previously unrecognised with conventional manometry.

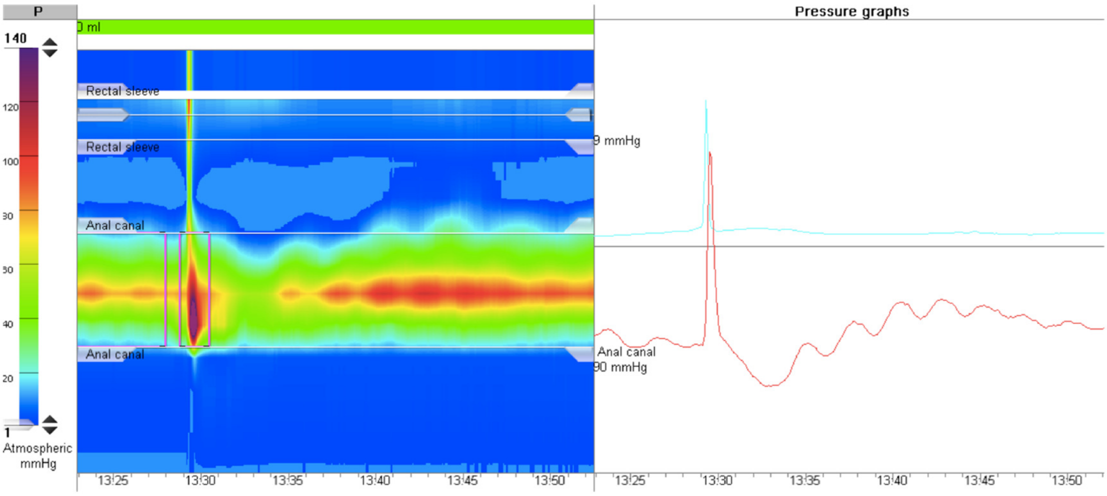

Figure 5-XI Representative HRAM colour contour plot and corresponding line trace (rectal pressure in blue above, anal pressure in red below) from a volunteer during a cough. During the manoeuvre anal pressures are seen to rise above rectal pressure. Following cough there is a rebound relaxation of the anal canal that recovers after a period of approximately 5 seconds.

5.5 Discussion

Anal manometry is the most widely used physiological test of anorectal function and in current practice can be performed using a variety of techniques. To date, experts have failed to reach consensus with regard to either the optimal test protocol or method of reporting, despite several 'position statements' and 'working party reports' being published on the topic (Keighley et al., 1989, Barnett et al., 1999, Azpiroz et al., 2002, Rao et al., 2002). A large share of this historic difficulty must be attributed to the paucity of appropriately large normative data sets (Rao et al., 1999, Chaliha et al., 2007, Jones et al., 2007, Noelting et al., 2012), all of which used variable methodology. Such a situation makes comparison between centres problematic, as it becomes difficult to determine whether an individual's test results are normal or abnormal, the endpoint of any clinically useful investigation.

One of the principal advantages of high resolution manometry is the ability to more clearly display pressure events within the structure of interest (Noelting et al., 2012). Colour contour plots provide a more intuitive understanding of pressure profiles and synchronized events over time than traditional line traces (Clouse et al., 2000, Ghosh et al., 2006b). When applied to the anorectum, the ability to observe this structure as a single unit is likely to allow the practitioner to more accurately appreciate the subtleties of co-ordinated anorectal events during a variety of manoeuvres (Ratuapli et al., 2012). The introduction of HRAM now presents an opportunity, similar to that of the Chicago process (Bredenoord et al., 2012) (which has revolutionised the use of manometry in the upper GI tract), to reach consensus regarding standardisation of this new and promising technique. Such consensus may then avoid the pitfalls that have bedevilled standard ARM (and all other tests of anorectal function).

5.5.1 Methodological limitations

The author acknowledges the following limitations: first, the dataset only included a small number of healthy male subjects and although this cohort more seldom presents for investigation, recent epidemiological studies may suggest that symptoms (such as faecal incontinence) in this group are more common than previously recognised (Whitehead et al., 2009a, Burgell et al., 2012).

Secondly, the author did not consistently perform endoanal or other structural investigations of sphincter integrity in this healthy volunteer cohort and therefore asymptomatic structural abnormalities of the sphincter complex (especially in the parous female cohort) cannot be excluded.

Thirdly, clinical application of the results of HRAM will require contextualisation within the overall clinical picture, alongside the results of other diagnostic tests.

Fourthly, it should be appreciated that, as a standardised protocol fro HRAM was being developed at the time of this study, 50 participants underwent an extended protocol which included a 5 minute period of familiarisation and 5 squeeze manoeuvres. Although the analysis in Chapter 4 suggested otherwise, it is not inconceivable that this may have had an effect on the end results. Results should therefore be interpreted with this protocol difference in mind.

Additionally, apart from the manual marking of the beginning and end of each manoeuvre, the integrated computer software generated measurement data automatically. This presents a number of implicit limitations. Although algorithms to generate these measurements have been designed in conjunction with clinicians, it remains possible that in some instances data do not adequately describe clinically important differences between individuals. For example, as data is collected and analysed at a rate of 10 Hz, a maximum absolute squeeze increment of 150mg that was sustained for one tenth of a second would be considered ‘equal’ to one sustained for 5 seconds. The implications of such a form of analysis and agreement with clinician derived values deserved further study.

Finally, the author accepts that the sample size for this study was based on feasibility rather than for the purpose of detecting differences in physiological parameters between groups. Results should therefore be interpreted with an appropriate level of caution. Post hoc sample size testing for variables of mean resting pressure and average incremental squeeze pressure confirms low power to detect differences, given the distribution of the cohort (ratio males : females; parous : nulliparous) and wide standard deviations. For example, mean resting pressures males *vs.* females, power = 30%; squeeze pressures males *vs.* females, power = 22%, resting pressures nulliparous *vs.* parous, power = 46%; mean squeeze incremental pressures nulliparous *vs.* parous, power = 69%.

5.5.2 Comparison with other healthy volunteer datasets

Comparisons of the findings from this study with previously published literature in healthy cohorts (n = >50 subjects) are summarised in Table 5-XIII.

Summary table of previous studies

Author	Ref	Year	Manometry type	System type	Catheter configuration ⃠ (mm)	channel N	spacing	N	sex	Anal resting pressure (mmHg)	Average squeeze increment (mmHg)
Poos	1	1986	Conventional	Balloon	2	1	n/a	72	F	50±3[a]	120±11[ab]
								103	M	54±3[a]	121±11[ab]
Pedersen	2	1989	Conventional	Water perfused	2	3	equally spaced radially	23	F	46 (40-58)[c]	103 (78-190)[bc]
								35	M	60 (51-98)[c]	163 (76-234)[bc]
Felt-Bersma	3	1991	Conventional	Water perfused	n.s.	4	n.s.	40	F	63±19[a]	102±36[a]
								40	M	68±21[a]	183±73[a]
Cali	4	1992	Conventional	Water perfused	n.s.	8	equally spaced radially	21	NF	75[de]	114[bde]
								18	PF	60[de]	103[bde]
								20	M	75[de]	144[bde]
Chaliha	5	2007	Conventional	Solid state	n.s.	n.s	n.s	283	NF	59±15[a]	107±28[a]
Corsetti	6	2010	Conventional	Water perfused	4.7	7	variable[f]	22	NF	73±16[a]	185±66[ab]
								30	M	82±15[a]	243±53[ab]
Gundling	7	2010	Conventional	Water perfused	4.8	8	n.s.	72	F	54 (17-126)[g]	151 (64-418)[g]
								74	M	67 (30-142)[g]	201 (69-413)[g]
Schuld	8	2012	Conventional	Solid state	3.3	1	n/a	66	F	63 (58-69)[c]	114 (106-212)[c]
								106	M	68 (63-72)[c]	137 (132-142)[c]
Li	8	2013	Hi-resolution (3D)	Solid state	10	256	4mm axial	46	F	60 (56-65)[c]	167 (151-184)[bc]
							2mm radial	64	M	61 (57-66)[c]	195 (181-209)[bc]
Noelting	9	2013	High-resolution	Solid state	4.2	8	6mm axial	30[h]	F	88±3[j]	73±6[j]
								32[i]	F	63±5[j]	96±12[j]
Carrington	10	2013	High-resolution	Solid state	4	10	8mm axial	34	NF	66 (46-111)[g]	130 (39-271)[g]
								62	PF	62 (25-107)[g]	92 (20-281)[g]
								19	M	67 (38-136)[g]	124 (40-474)[g]

Legends overleaf

n.s. not specified; n/a not applicable; F = females; M = males; NF = nulliparous females; PF = parous females
a. mean ± SD
b. reported as absolute maximum squeeze pressure, not increment
c. median (95% CI)
d. mean
e. reported as cmH_20 but converted to mmHg in this table for purposes of comparison ($1cmH_20$ = 0.7356 mmHg)
f. 4 radial ports at 5cm with 1 port 5mm proximally and 1 port 5mm distally
g. reported as median (range)
h. age <50
i. age >50
j. reported as mean ± SEM

References (1) (Poos et al., 1986) (2) (Pedersen and Christiansen, 1989) (3) (Felt-Bersma et al., 1991) (4) (Cali et al., 1992) (5) (Chaliha et al., 2007) (6) (Intestinale, 2010) (7) (Gundling et al., 2010) (8) (Li et al., 2013) (9) (Noelting et al., 2012) (10) (in press)

Table 5-XIII Summary table of previous studies exploring anal resting and squeeze function in health using anal manometry. Studies with >50 participants have been included. The mean resting pressure and mean squeeze increments reported here are seen to be very similar to those reported by Gundling *et al* in 2010 (who performed a study of conventional water perfused manometry in 72 women and 74 men using an 8 lumen, 15F water perfused manometry catheter) (Gundling et al., 2010) however squeeze pressures appear to significantly higher than those reported recently by Noelting *et al* in 2013 (using the Manoview system in 62 females) (Noelting et al., 2012).

There are several possible reasons for these observed differences. First, it is generally agreed that equipment set-up is likely to have an impact on absolute reported values as (for example) water perfused manometric systems are generally regarded to have lower fidelity than those that utilise solid-state technology (Varma and Smith, 1984, Florisson et al., 2006, Scott and Gladman, 2008). Secondly, data from previous studies may reflect a cohort with different demographics (the relationship between age and parity on anorectal function is well documented) (Poos et al., 1986, Jameson et al., 1994, Gundling et al., 2010). Thirdly, as anal manometry is a dynamic investigation partly of voluntary function, it is well appreciated that nuances of study protocol are likely to impact derived results (Schouten and van Vroonhoven, 1983, Rao et al., 1999, Rao et al., 2002, Heinrich et al., 2013). Indeed, a recent study in 70 patients with defaecatory dysfunction demonstrated that enhanced instruction and verbal feedback significantly improved squeeze pressures when compared to standard instruction (Heinrich et al., 2013). It is certainly conceivable that this may account for some of the differences during comparison with previous studies.

5.5.3 Description of normality

This study aimed to develop normal value ranges for traditional measures of anal function as described by HRAM. This raises an interesting philosophical question as to the exact description of normality.

It is appreciated that a number of demographic features (including age, sex and BMI) impact on measurable features of anorectal function, particularly parity (Poos et al., 1986, Felt-Bersma et al., 1991, Cali et al., 1992). Several series have demonstrated that childbirth affects anal sphincter function (Donnelly et al., 1998, Fynes et al., 1999, Oberwalder et al., 2003) however childbirth is a normal physiological event. It is therefore reasonable to postulate about whether a parous female truly has 'normal' sphincter function.

There are two viewpoints in this argument. One could take the approach that, as age and parity are associated with a reduction in parameters of sphincter function, only young nulliparous females should be considered to have 'normal' anal sphincters. This approach however seems somewhat disproportionate as some degree of occult sphincter injury is seen in a high proportion of vaginal deliveries without development of symptoms.

The alternative approach, (that was taken in this thesis) is to demographically match asymptomatic controls according to parity assuming that some reduction in some measures of anal sphincter function are physiological.

5.5.4 Implications of this study

Although in this study sample size was based on feasibility without formal sample size calculation, (and differences reported between demographic groups should therefore be interpreted with caution), the already appreciated reduction in sphincter function associated with parity (Boyle et al., 2012) has, however, once again been highlighted in this dataset. It is possible that further longitudinal investigation of healthy parous females with poor sphincter function using HRAM may prove useful, particularly given the fact that onset of incontinence commonly occurs up to 2 decades following obstetric trauma, at around menopausal age (Lunniss et al., 2004).

Examination of the reference ranges presented in this study demonstrates that at least 4 traditional measures (residual push pressure, maximum rectal push pressure, rectoanal gradient and endurance squeeze duration) are unlikely to have diagnostic utility in their current form due to wide variations in health. This highlights the fact that traditional metrics themselves have limitations and indicates the need for new parameters of anal function. This study particularly highlights deficiencies in current measures used for the definition of dyssynergia. Were currently accepted definitions for dyssynergia applied to this cohort of healthy volunteers (i.e. the presence of a negative recto-anal gradient is indicative of defaecatory dysfunction (Noelting et al., 2012)), 33 (28%) of individuals would have been classified as having an abnormal result. Whether such a large proportion of asymptomatic individuals should be classified as having an abnormal test result (or whether the test itself should change) is a philosophical question that requires further investigation.

In the upper GI tract, the application of high resolution manometry has led to the development of several novel parameters such as the distal contractile integral and integrated relaxation pressure of the lower oesophagus, both of which have led to changes in the classification of oesophageal dysmotility (Bredenoord et al., 2012).

On this basis, the second part of the current study explored qualitative findings in sphincter function that may subsequently be shown to have disease relevance. A number of novel phenomena were observed, including the presence of post-cough relaxations in some individuals. Further exploration of this may be interesting, as the presence of this feature in those with poor sphincter tone may be an important feature in the pathophysiology of faecal incontinence. Qualitative observations also included synchronous recordings of rectal pressure acknowledging that disturbances of defaecatory function usually represent the summation of anal and rectal dysfunction (and often colon) (Palit et al., 2012).

5.6 Conclusions

This study presents results of a large (to the author's knowledge, largest within the literature) healthy volunteer dataset with studies performed using a standardised HRAM protocol, which will hopefully provide a starting point for discussion, collaboration and ultimately standardisation of this widely used technique.

Further studies in health and disease using short and prolonged duration studies are underway to determine the clinical significance of these findings and their incorporation to a future recording protocol.

5.7 References

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Chapter 6

6 Anal sphincter profiles: development and analysis of a novel instrument for assessment of anal motor function using high resolution anorectal manometry (HRAM)

6.1 Rationale

It is widely accepted that anal sphincter dysfunction is an important pathophysiological mechanism in the generation of symptoms of fecal incontinence (FI) (Bielefeldt et al., 1990, Kamm, 1994, Lunniss et al., 2004, Rao, 2004, Bharucha et al., 2005, Rao et al., 2016b) though pathophysiology is recognized to be multifactorial in the majority of sufferers (Rao, 2004, Bharucha et al., 2015, Townsend et al., 2016). The most common investigation for interrogation of sphincteric function is anorectal manometry (Barnett et al., 1999, Azpiroz et al., 2002, Bharucha, 2006b, Scott and Gladman, 2008, Rao et al., 2016b). This method of recording mechanical activity of the anal sphincter through measurement of changes in intraluminal pressure has been applied to clinical practice since it was described in the early 1960s (Schuster et al., 1963, Phillips and Edwards, 1965, Duthie and Watts, 1965).

Due to technological constraints, the assessment of anorectal pressures has until recently, been performed through utilization of manometric catheters that incorporate a limited number of pressure sensors (Sun and Rao, 2001, Rao et al., 2002, Scott and Gladman, 2008) with resultant data displayed as line traces and expressed as point pressures at levels from the anal verge. This traditional method for data collection and display is often termed '*conventional* anal manometry' (CAM). Despite being the only recommended first-line investigation for FI (Rao et al., 2016b) and in widespread use (Rao et al., 2002, Scott and Gladman, 2008), the utility of CAM has been questioned, as there is considerable overlap of findings between health and disease (Bharucha et al., 2005, Lam et al., 2012), little evidence that results act as a robust indicator of disease severity (Hill et al., 1994, Engel et al., 1995, Bharucha et al., 2005, Bordeianou et al., 2008, Wickramasinghe et al., 2015) and even less evidence that findings influence clinical management or predict treatment outcomes (Vaizey and Kamm, 2000, Bharucha, 2006b, Wald, 2006, Norton et al., 2007). Nevertheless, some international guidance places anorectal manometry as a screening (go-no-go) investigation for further evaluation of patients with FI (Rao et al., 2016b).

Recently, technological advances have enabled development of manometric catheters that collect data from an increased numbers of sensors with display and analysis of results in a format that allows a more global appreciation of structure and function. Current commercial systems available for clinical use incorporate catheters that contain between 12 - 257 individual sensors. Any manometric system which displays data in this way from such sensors spaced <0.8 cm apart is termed '*high-resolution* or *high-definition* manometry'. Although relatively novel in its application to the anorectum, high-resolution techniques have revolutionised the understanding of motility within the esophagus (Miller et al., 1988b, Cornes et al., 1991) with several studies demonstrating that the reduced inter-sensor distance and innovative display offers significantly improved diagnostic yield and accuracy over conventional manometry (Fox et al., 2004, Hansen et al., 2006). For this reason, high resolution oesophageal manometry is now widely accepted as the gold-standard method for investigation of esophageal motor function (Bredenoord et al., 2012).

Although a number of potential advantages of high-resolution anorectal manometry (HRAM) have been cited (Lee et al., 2013, Vitton et al., 2013b, Dinning et al., 2016), the technique is at a much earlier stage of adoption than for esophageal evaluation. At the time of submission of this thesis, only 45 original articles have been published in the scientific literature. Of these, only 3 have explored potential advantages over CAM (Jones et al., 2007, Vitton et al., 2013b, Kang et al., 2015).

To the author's knowledge, there has been no study to date that conclusively demonstrates a diagnostic advantage of HRAM over CAM. At the time of writing this thesis, there has been no study to date that conclusively demonstrates a diagnostic advantage with this novel technique. Despite this, the uptake of HRAM has begun to increase. Chapter 2 of this thesis demonstrates that 14/62 (23%) of institutions that have moved from CAM to HRAM (Carrington et al., 2015).

6.2 Aims

The aims of this study were several-fold: (1) to develop a novel method for analysis of voluntary (squeeze) and involuntary (resting) anal sphincter function using HRAM; (2) in patients with FI, to assess diagnostic accuracy of these new measures in comparison with CAM in terms of discriminating health status from healthy volunteers (HV); (3) in patients with FI, to evaluate the responsiveness of these novel measures (compared to CAM) to changes in patient phenotype notably by measuring their utility to a) predict anal sphincter defects and b) symptom severity; and (4) to measure agreement and diagnostic yield between CAM and novel HRAM tests and thus describe a cohort of patients, who using previous manometric measures might have been denied further investigation on the basis of a normal test result (Rao et al., 2016a).

6.3 Existing methods of reporting of rest and squeeze using conventional anal manometry

6.3.1 Conventional anal manometry resting average (CAM-RA)

As discussed previously, conventional anal manometry is poorly standardized. Typical practice is to perform either stationary, station pull-through or pull-through manometry (Rao et al., 2002, Scott and Gladman, 2008) with typically a maximum of 5 readings taken from the longitudinal length of anal canal.

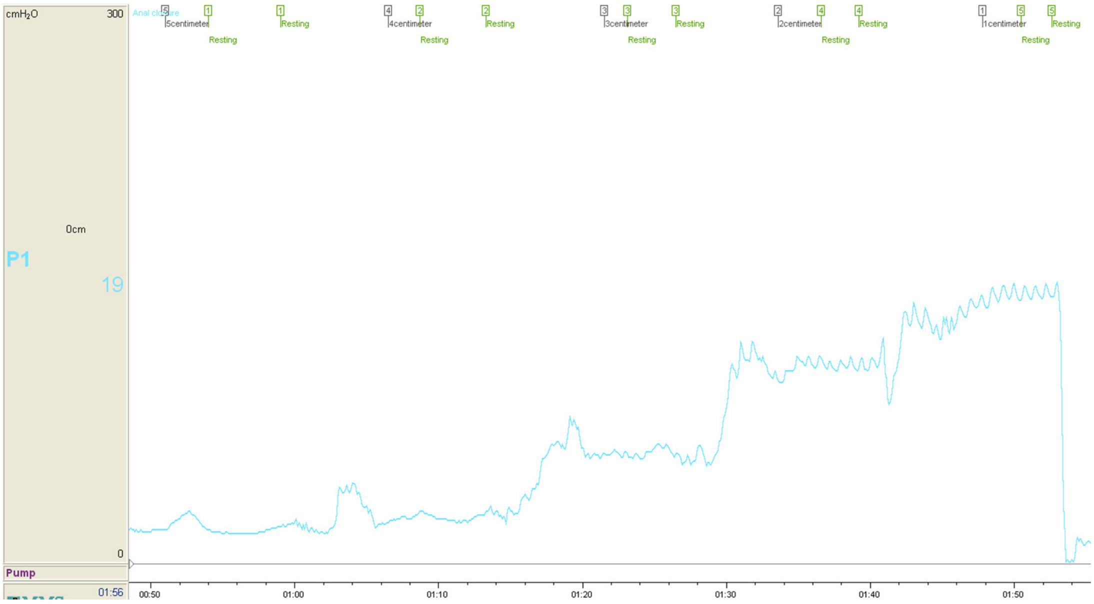

Figure 6-I Example line trace from an anal manometry study. The anal pressure at rest is measured at different levels of the anal canal. The average pressure at each level is reported.

During the assessment of rest, the average absolute pressure over a given period of time is reported (example Figure 6-I). For the purpose of this chapter this will be referred to as the conventional anal manometry resting average (CAM-RA). The exact methods of reporting are poorly described in the literature (for further analysis of variation in practice between UK centres, see previous chapters). Reporting may be of pressures at a number of levels within the anal canal (typically 5cm, 4cm, 3cm, 2cm and 1cm from the anal verge) or may simply be the single maximum value within the anal canal (Rao et al., 2002).

Should a single maximum average value be reported, significant assumptions must be made during result interpretation due to extrapolation that this single value is representative of the function of the anal canal as a whole.

6.3.2 Conventional anal manometry squeeze increment (CAM-SI)

For assessment of squeeze, a similar approach is taken, with measurements at intervals (typically 1cm) through the anal canal (Figure 6-II).

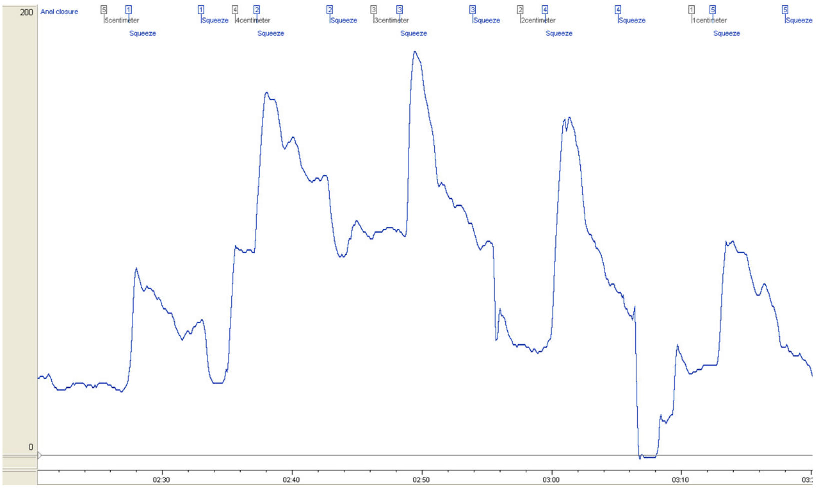

Figure 6-II Example line trace from an anal manometry study. Changes in intra-anal pressure are recorded during five voluntary squeezes, with the point of measurement at different levels of the anal canal (squeeze 1 at 5cm from the anal verge with each squeeze performed with the recording channel 1cm moved 1cm distally).

Either the absolute, incremental, maximum or sustained pressure can be reported (Fighre 6-III). Duration of the squeeze maneuver is likewise unstandardized and may vary from 5 – 30 seconds (Felt-Bersma et al., 1991, Rao et al., 1999, Gundling et al., 2010). The single maximum value recorded from the anal canal is then usually reported (Rao et al., 2002).

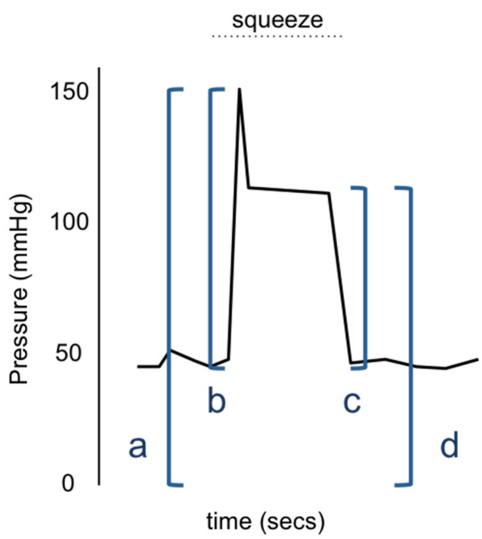

Figure 6-III Diagrammatic representation of possible interpretations of squeeze during conventional anal manometry (a) = absolute maximum squeeze increment, (b) incremental maximum squeeze increment; (c) incremental sustained squeeze increment (d) absolute sustained squeeze increment.

There are a number of limitations associated with this technique. First, appreciation of coordinated anorectal events is impossible as only a single point within the anal canal is measured at each point in time. Secondly, significant assumptions must be made during result interpretation due to extrapolation that this single value is representative of the function of the anal canal as a whole. Thirdly, the definition of a 'sustained' increment is subjective, and may easily lead to reporting bias.

6.4 Existing reporting methods of rest and squeeze with high resolution anal manometry

6.4.1 HRAM resting average (HRAM-RA)

As with CAM, there is no existing standard for the reporting of HRAM resting data. Analysis is typically performed with the assistance of in-built software that varies according to individual system specifications (Jones et al., 2007, Noelting et al., 2012, Vitton et al., 2013b, Carrington et al., 2014a).

During the reporting of anal resting pressure, the HRAM system used within the institution associated with this thesis (Solar GI HRM v9.1, Medical Measurement Systems [MMS], Enschede, Netherlands) allows selection and subsequent analysis of data from of an area of interest (named the 'e-sleeve'). The software then selects and reports the highest reading from this area of interest onto a representative line trace at a rate of 10Hz (Figure 6-IV).

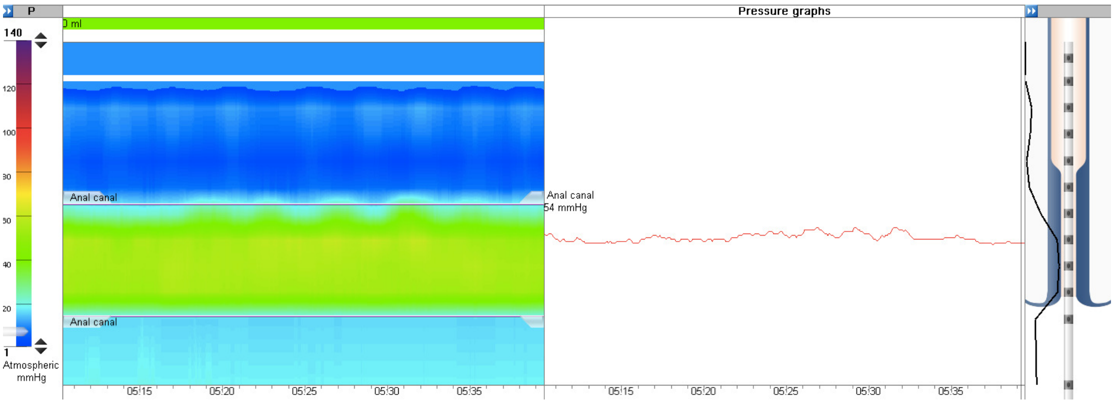

Figure 6-IV Representative 30 second line trace from a healthy volunteer during rest. On the left panel, the moderate pressures within the anal canal are represented as a band of green/yellow with the lower rectal pressures represented as blue above. The pressure graph in the right panel represents the maximum pressures within the e-sleeve box. The 'HRAM average anal resting pressure' s calculated as an average of these pressures over the period of interest.

The practitioner determines the duration of analysis and a calculation of the average of these highest readings is then reported. This is termed the HRAM resting average (HRAM-RA).

This new method has limitations. Despite the fact that data is collected from multiple sensors within the anal canal, the final analysis once more only incorporates data from the single point of maximal pressure at each moment in time.

6.4.2 HRAM squeeze increment (HRAM-SI)

Similar to assessment of resting pressure, during analysis of squeeze, the 'e-sleeve' box is placed over the area of interest allowing the software to then select and reports the highest incremental reading from this area of interest onto a representative line trace at a rate of 10Hz (Figure 6-V and Figure 6-VI). This is termed the HRAM squeeze increment. (HRAM-SI).

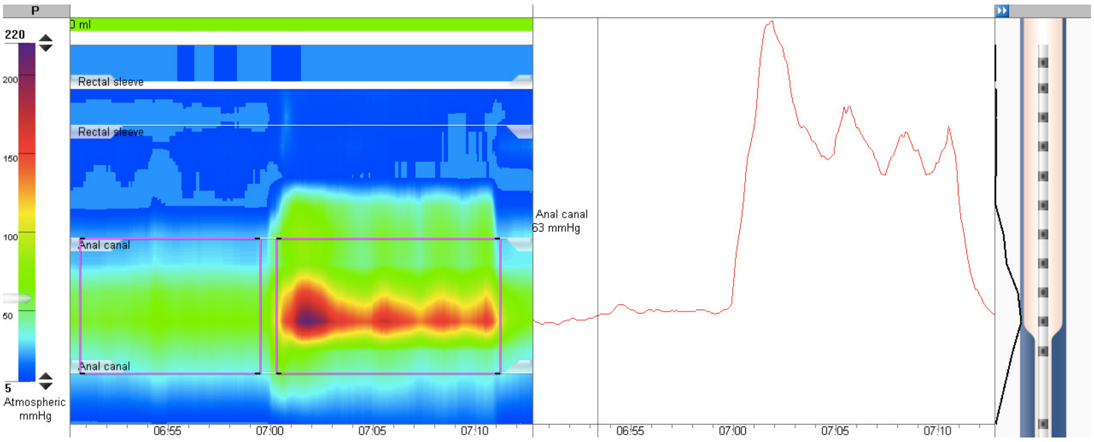

Figure 6-V Representative colour contour plot and associated line trace from a squeeze maneuver in a healthy individual using HRAM. The anal canal is seen as a band of green at rest and is selected within the 'e-sleeve' (dark red rectangular box). During the voluntary squeeze the pressure within the anal canal increases, reflected as a change in colour from green to red. A corresponding change is seen in the line trace. The software automatically analyses the average incremental difference in pressures between the resting and squeeze e-sleeve boxes and reports an average squeeze increment.

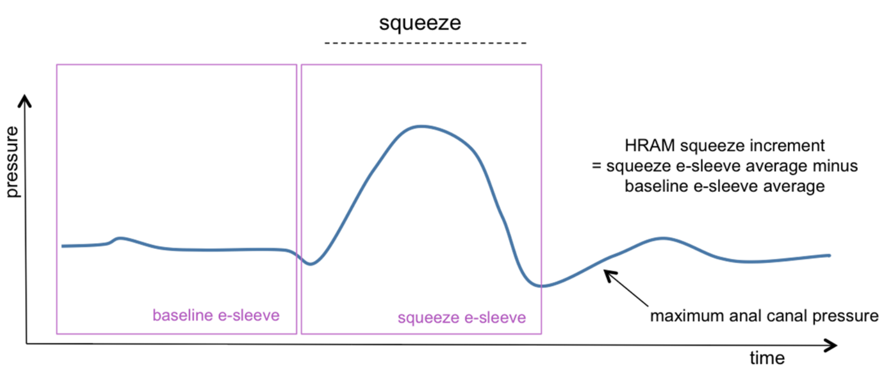

Figure 6-VI Diagrammatic representation of method for calculation of HRAM squeeze increment.

This new method presents limitations. Despite the fact that data is collected from multiple sensors within the anal canal and that global sphincter activity can be appreciated by subjective inspection of the colour contour plot, the final analysis once more only incorporates data from the single point of maximal pressure at each moment in time.

Furthermore, average values will differ depending on the length of the squeeze i.e. it is likely that a squeeze sustained for 3 seconds will have a higher average value that one sustained for 10 seconds. This has implications due to variation in practices between centres.

6.5 Proposed novel measures of rest and squeeze utilizing high resolution anal manometry

Following appreciation of the limitations of existing measures, a novel form of analysis of HRAM data was conceived. Termed a 'profile' analysis, this measurement incorporated activated sphincter length, absolute pressure, and (in the context of a voluntary manoeuvre such as squeeze) duration of the event.

6.5.1 HRAM resting profile (HRAM-RP)

As illustrated in previous chapters, there is significant variation in the manometric morphology of the anal (

Figure 6-VII). This suggests that anal canal length, in addition to the absolute pressures generated may be important in the maintenance of continence.

A novel manometric variable was created and termed the HRAM resting profile (HRAM-RP). To produce this measurement, the average pressure from all sensors within the anal canal over the 30-second period of rest squeeze was multiplied by the anal canal length. The resultant value was reported in mmHg.30s.

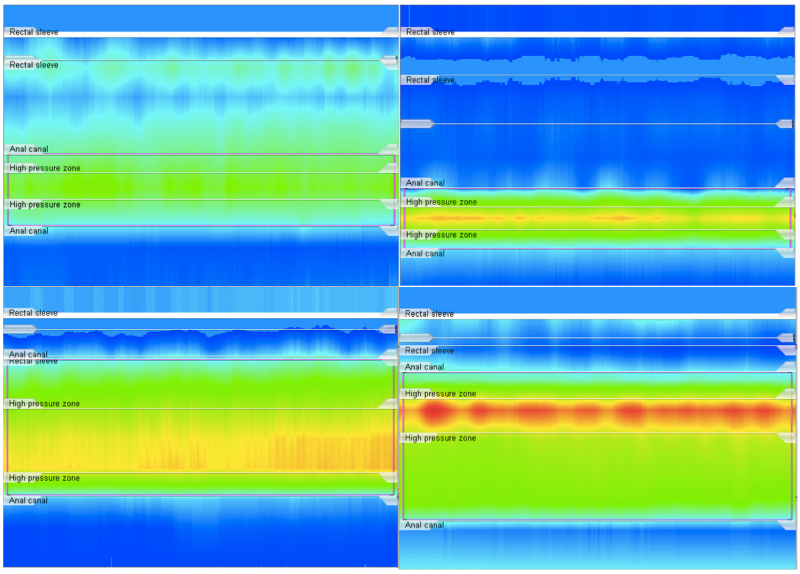

Figure 6-VII Representative colour contour plots from 4 healthy volunteers during rest demonstrating differences in manometric sphincter morphology.

As this measure takes into account pressure, maneuver sustainability and sphincter length, the author proposes that this 'profile' measure is the truest reflection of anal sphincter function, and that it will more clearly describe alteration of sphincter function where it exists.

6.5.2 HRAM squeeze profile (HRAM-SP)

Similar to patterns seen during analysis of anal resting pressure, during analysis of squeeze, there is significant variability, not only in the ability to sustain a voluntary squeeze, but also of the degree of anal canal that is responsible for the resultant change in pressure in health (Figure 6-VIII)

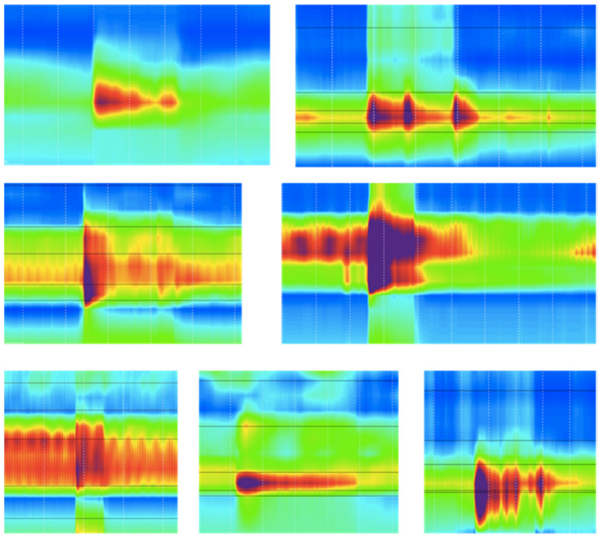

Figure 6-VIII Representative colour contour plots from 7 healthy volunteers during a voluntary squeeze demonstrating differences in morphology of sphincteric response during the manoeuvre.

It is appreciated that a reduced functional anal canal length (FACL) is associated with faecal incontinence (Nivatvongs et al., 1981b, Jorge and Wexner, 1993, Scott and Gladman, 2008) and for this reason remains a standard variable reported during conventional manometry. Despite this, the contribution of sphincter volume is not accounted for in measures that report the single point of maximum function. This lessens a significant advantage of HRAM, which is the ability to take simultaneous measurements from multiple areas of the anal canal, and may lead to incorrect assumptions regarding true anal sphincter function (Figure 6-IX).

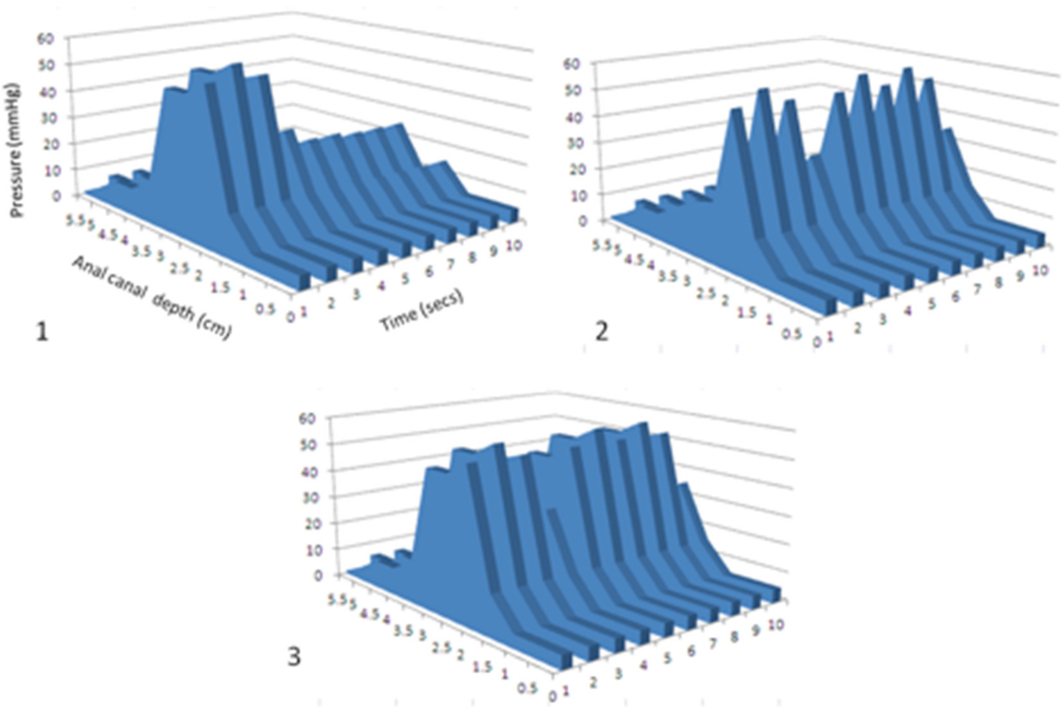

Figure 6-IX Three-dimensional volume plots representing hypothetical values that may be obtained during a squeeze maneuver. In each example maximum squeeze increment would be identical (and thus using conventional measures would be reported as such) however morphology clearly differs. Plot (1) demonstrates a poorly sustained increment that involves a long anal canal segment. Plot (2) demonstrates a well-sustained increment, which is representative of contribution from a single point within the anal canal. Plot (3) demonstrates a well-sustained squeeze, involving a long anal canal segment.

When high-resolution manometry is applied within the oesophagus, a calculation exists, which takes into account length, vigor and persistence of distal oesophageal contraction during a swallow. This is known as the Distal Contractile Integral (DCI) and has formed one of the cornerstones of the Chicago Classification (Ghosh et al., 2006a, Kahrilas et al., 2008).

The author proposes a similar calculation for use within the anal canal, termed a squeeze profile (HRAM-SP). This calculation takes into account the average pressure measured by all manometric sensors within the anal canal, the anal canal length, and the duration of the squeeze manoeuvre.

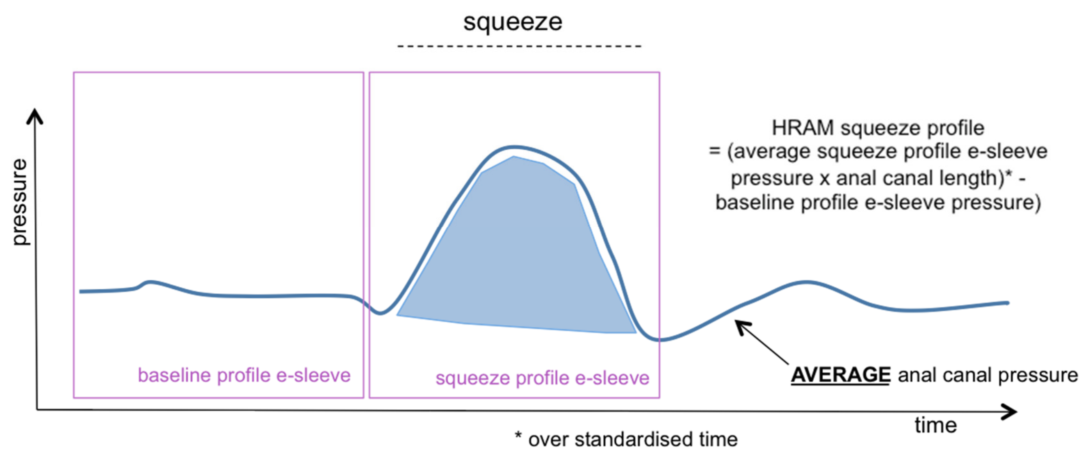

Figure 5-VIII Diagrammatic representation of method for calculation of the HRAM squeeze profile.

As this measure takes into account pressure, maneuver sustainability and sphincter length, the author proposes that the HRAM-SP measure is the truest reflection of anal sphincter function, and that it will more clearly describe alteration of sphincter function where it exists.

Values were expressed as mmHg.cm.5sec for short squeezes and mmHg.cm.30sec for the endurance squeeze measurement.

6.6 Methods

6.6.1 Subjects

6.6.1.1 Healthy controls

Eighty-five healthy female subject were recruited from the London School of Medicine and Dentistry, London. Ethical approval was granted by the Queen Mary University Research Ethics Committee (ref QMREC 2010/74 and QMREC 2013/12).

The following exclusion criteria were applied:

1. Symptoms of defaecatory dysfunction, particularly those of faecal incontinence or constipation (as assessed by modified Vaizey score [>5] (Vaizey et al., 1999) and Cleveland Clinic constipation score [>8] (Agachan et al., 1996) respectively);
2. History of previous anorectal surgery;
3. Use of medications that may affect anorectal function;
4. Inability to provide informed consent;
5. Inability to communicate effectively in English.

All individuals underwent a general and focused clinical history (including obstetric history) and examination. There was no formal assessment of anal sphincter morphology in this group.

6.6.1.2 Patients with faecal incontinence

Ninety-five consecutive female patients with a primary presenting complaint of FI underwent HRAM as part of routine anorectal physiology investigation in the GI Physiology Unit, The Royal London Hospital.

A general and focused clinical history determined symptoms of defaecatory dysfunction. The presence or absence of symptoms of passive incontinence, urge incontinence and/or post defaecatory leakage were noted. A full obstetric history was taken. FI symptom severity was assessed using the modified Vaizey score and those with a score of <6 were excluded from analysis. Endoanal ultrasound (10mHz transducer, B-K Medical, Berkshire, UK) was performed in all patients (Eckardt et al., 1994) and anal sphincter morphology was reported by a senior clinician with >10 years' experience in results interpretation.

6.6.2 Manometric protocol

All participants (HV and FI) underwent an identical manometric protocol (as outlined in Chapter 3). Briefly, before each study, the catheter was immersed in tepid water for 3 minutes. Sensors were then calibrated to atmospheric pressure. The participant was given the opportunity to defecate if required prior to investigation. Bowel preparation was not used. All participants were studied in the left-lateral position with knees and hips flexed to 90 degrees. Prior to catheter insertion, a clinical examination of the perineum was performed. This included digital rectal examination during which participant understanding of the command “squeeze” was confirmed, using the phrase “squeeze up and in as though you are trying to stop yourself going to the toilet”(Carrington et al., 2014a) .

All test manoeuvres were performed in accordance with published international minimum standards(Rao et al., 2002). The manometric catheter was inserted into the anorectum with the distal 2 microtransducers visible (the second most distal being located immediately outside of the anal verge). Following a 3-minute run-in period for the purposes of stabilization, manoeuvres were performed in a standard sequence with a 30 second recovery period incorporated between each manoeuver. For examination of anal resting pressure (rest), the participant was asked to relax and remain quiet for a period of 60 seconds. For examination of voluntary sphincteric function (squeeze) the participant was asked to “squeeze up, in and hold” as previously practiced for a period of 5 seconds. For examination of voluntary sustained sphincteric function (endurance squeeze) the participant was asked to squeeze and hold for 30 seconds. The squeeze manoeuvre was performed twice (second squeeze used for analysis), the endurance squeeze manoeuvre was performed once. (Rao et al., 2002).

6.6.3 Offline analysis

For each study, data for rest and squeeze were analysed offline, first using embedded manometric software (v9.1 MMS/Laborie) and then using bespoke measurements conceived by the author, with algorithms written by a software engineer. This generated a total of 7 manometric variables (3 expressing data for rest and 4 expressing data for squeeze). HRAM methods utilised data from all manometric sensors. CAM analysis was performed using a sub-sampling technique, using only data from the sensor recording the highest absolute pressure within the anal canal (mimicking standard pull-through methods(Scott and Gladman, 2008)).

6.6.4 Manometric variables

The following parameters were calculated:

1. CAM resting pressure (CAM-RA)
2. HRAM resting average (HRAM-RA)
3. HRAM resting profile (HRAM-RP)
4. CAM squeeze increment (CAM-SI)
5. HRAM squeeze increment (HRAM-SI)
6. HRAM 5 second squeeze profile (HRAM-SP-5)
7. HRAM 30 second squeeze profile (HRAM-SP-30)

6.7 Results

6.7.1 Subjects

Participant age was normally distributed for both the control (skewness of -0.19 [*SE* = 0.210] and kurtosis of -0.992 [*SE* = 0.417]) and patient group (skewness of -0.19 [*SE* = 0.247] and kurtosis of -0.966 [*SE* = 0.490]). The patient group were significantly older than the control group: patient mean age 55.1 ± 16.4 years *vs.*

control mean age 41.6 ± 12.6 years (95% CI, -17.5 to -9.5), $t(169) = -6.7$, Independent sample T test $p < .0001$.

As expected, patients with faecal incontinence had significantly higher symptom severity scores than controls with symptom severity data in the patient group being positively skewed (skewness of 0.589 [*SE* = 0.247] and kurtosis of -0.537 [*SE* = 0.490]). The median Vaizey score in the patient group was 11 (IQR 7) *vs.* 1 (IQR 1) in the control group (Independent Samples Mann-Whitney U test $p < .001$).

With regards to obstetric history, a significantly greater proportion of patients (80%) were parous when compared to controls (55.6%) – Fisher's exact Test $p < .001$.

In the patient group, there was evidence of an underlying external anal sphincter abnormality (defect, scarred or degenerate in appearance) in 57 (60%) individuals. The remaining 38 (40%) had normal anal sphincter anatomy. There was no difference in symptom severity between patients with sphincter defects (mean Vaizey score 12 ± 5) *vs.* those with normal anal sphincter anatomy (mean Vaizey score 12 ± 5), (95% CI, -1.96 to 1.86), $t(79) = -.55$, Independent sample T test $p = .956$.

6.7.2 Delineation of normal ranges for manometric parameters

Table 6-I displays descriptives for each squeeze measure in the healthy control group.

Healthy control descriptives								
		Resting measures			**Squeeze measures**			
		CAM-RA (mmHg)	**HRAM-RA (mmHg)**	**HRAM-RP (mmHg.cm.30sec)**	**CAM-SI (mmHg)**	**HRAM-SI (mmHg)**	**HRAM-SP-5 (mmHg.cm.5sec)**	**HRAM-SP-30 (mmHg.cm.30sec)**
Mean		66.5	64.624	167.604	95.8	139.8	589.1	430
95% CI	Lower	62.5	60.723	153.023	74.9	107.3	495	355.5
	Upper	70.5	68.524	182.184	116.7	172.3	683.2	504.5
Median		66.0	60	163.2	92	142	499.8	385
SD		18.5	18.0818	67.5958	45.9	71.3	206.7	163.6
Range		32 - 120	29 - 108	46.8 - 423.4	37 - 197	36 - 287	252 - 969.4	206.4 - 743.4
IQR		23.0	23	76.6	71.5	103	312.6	266
SEM		2.0	1.9612	7.3318	10	15.6	45.1	35.7
Skewness		0.6	0.7	1.0a	0.742[a]	0.539	0.742[a]	1.059[a]
Kurtosis		0.4	0.04	2.0b	0.04	-0.324	0.503	1.718[b]
5^{th} Percentile		36.2	39.6	71.1	43	29	254	191

a. Significant skewness (Z-score >±2.58)

b. Significant kurtosis (Z-score >±2.58)

Table 6-I Table of descriptives for conventional and HRAM measures of squeeze in healthy controls. N = 85. Blue shaded 5^{th} percentile determined as the lower limit of normality.

Visual inspection of representative dot plots for each measure (Figure 6-X) and calculation of Z skewness and kurtosis scores demonstrated that HRAM-RP, CAM SI, HRAM-SP-5 and HRAM-SP-30 were not normally distributed.

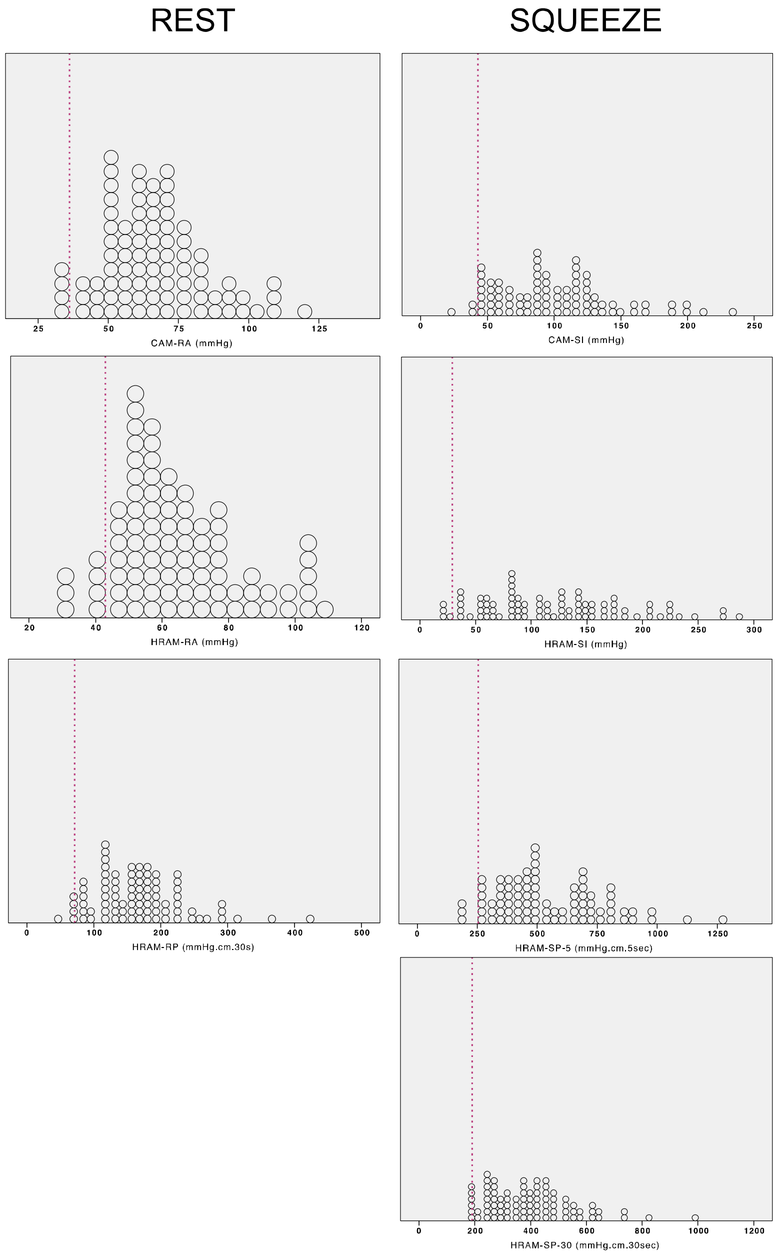

Figure 6-X Frequency dot plots for manometric measures of rest and squeeze. Pink dotted line represents the 5th percentile (determined as the lower limit of normality).

Consequently, the lower limit of normality for each measure was defined as the HV group 5th percentile (Table 6-I).

6.7.3 Comparison of resting and squeeze measures between healthy volunteers and patients with faecal incontinence

The practicality of the definition for limits of normality was checked by visual inspection of paired control and patient frequency histograms for each measure (Figure 6-XI).

Close scrutiny of these histograms demonstrates that for traditional measures, there appears to be significant overlap between the patient and control groups. For HRAM measures, overlap appears comparatively reduced. Particularly for the profile measures, the central point of the healthy group data appears to move closer towards the upper limit of the patient group with HRAM-SP-5 and HRAM-SP-30 subjectively appearing to possess the most discriminative ability.

Descriptives for the patient group are displayed in Table 6-II. Comparison of data distribution for all measures using the Mann-Whitney U test demonstrated that values in the patient group were lower than in healthy controls. This difference was significant for all measures and highly significant ($p < 0.001$) for HRAM-RA, CAM-SI, HRAM-SI, HRAM-SP-5 and HRAM-SP-30 (Table 6-III).

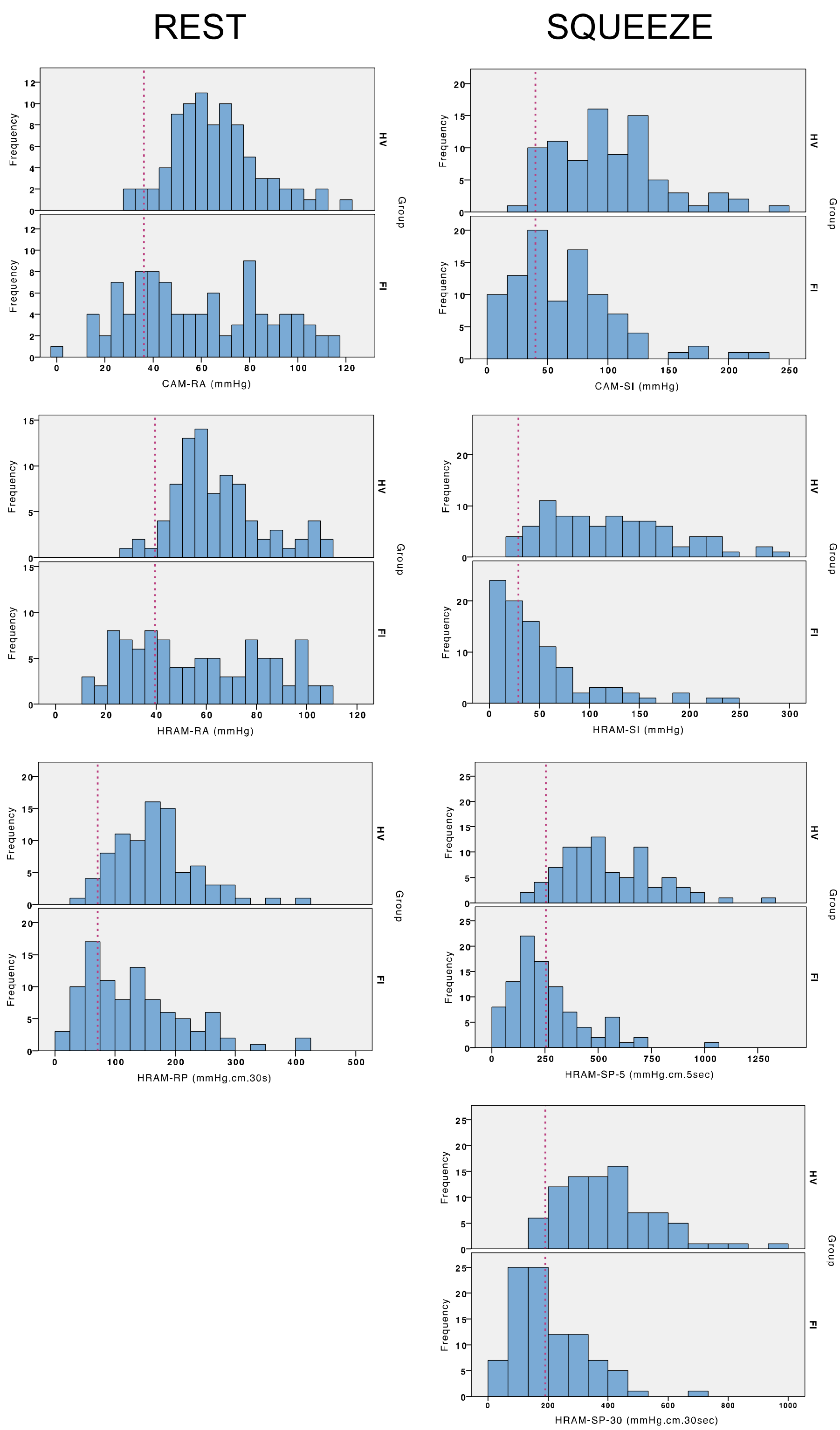

Figure 6-XI Frequency by percent histograms for manometric measures of rest and squeeze. The pink dotted line represents the lower limit of normal. N=85 healthy controls and N=95 patients with faecal incontinence.

Patients with faecal incontinence descriptives								
		Resting measures			**Squeeze measures**			
		CAM-RA (mmHg)	**HRAM-RA (mmHg)**	**HRAM-RP (mmHg.cm.30sec)**	**CAM-SI (mmHg)**	**HRAM-SI (mmHg)**	**HRAM-SP-5 (mmHg.cm.5sec)**	**HRAM-SP-30 (mmHg.cm.30sec)**
Mean		58.8	56.8	133.6	65	49.6	589.1	203.3
95% CI	Lower	53.0	51.3	116.4	56	39.3	495	178.7
	Upper	64.5	62.3	150.8	74	59.9	683.2	227.8
Median		55.0	55.0	122.4	61	38	499.8	172
SD		795.5	723.2	7112.5	44.3	50.7	206.7	120.5
Range		28.2	26.9	84.3	0 - 226	-242	252 - 969.4	29 - 678.4
IQR		0 - 115	13 - 110	15.3 - 405	71.5	103	312.6	266
SEM		47.0	45.0	117.4	4.5	5.2	45.1	12.4
Skewness		0.2	0.2	1.0[a]	1.130[a]	1.809[a]	0.742[a]	1.078[a]
Kurtosis		-1.0	-1.2	0.9	1.899[b]	3.562[b]	0.503	1.528[b]
5^{th} Percentile		15.8	18.6	28.5	4.8	1.6	51.4	44.98

a. Significant skewness (Z-score >±2.58)

b. Significant kurtosis (Z-score >±2.58)

Table 6-II Table of descriptives for manometric measures of rest and squeeze in patients with faecal incontinence. N = 95.

Healthy volunteer and patient with faecal incontinence comparison - Mann-Whitney U test						
		HV Median	IQR	FI Median	IQR	Sig
Resting measures	CAM-RA (mmHg)	66	23	55	47	*
	HRAM-RA (mmHg)	60	23	55	45	*
	HRAM-RP (mmHg.cm.30sec)	163.2	76.6	122	117.4	***
Squeeze measures	CAM-SI (mmHg)	92	71.5	61	71.5	***
	HRAM-SI (mmHg)	142	103	38	103	***
	HRAM-SP-5 (mmHg.cm.5sec)	499.8	312.6	219	312.6	***
	HRAM-SP-30 (mmHg.cm.30sec)	385	266	172	266	***

* Statistically significant; $p < .05$

*** Highly statistically significant; $p < .0001$

Table 6-III Comparison of manometric measures for rest and squeeze in healthy control and patients with faecal incontinence. A Mann-Whitney U test was used to assess differences between groups. A *p* <. .05 was considered statistically significant.

6.7.4 Validation of HRAM measures and comparison with CAM measures

The preliminary analysis above (chapter 6.7.3) suggests that novel HRAM measures of rest and squeeze function appear to have at least a similar ability as conventional measures to identify reduced anal sphincter function associated with symptoms of faecal incontinence. Validation of these findings was further explored with receiver operator curve analysis, correlation with symptom severity and regression analysis.

6.7.4.1 Chi Squared analysis – classification of 'normal anal sphincter function' in patients with faecal incontinence and healthy controls using CAM and HRAM measures

A Chi-square (χ^2) analysis was performed to determine the association between participant group (i.e. healthy control *vs*. patient with faecal incontinence) and sphincter function status (i.e. 'normal anal sphincter function' *vs.* 'abnormal anal sphincter function') as determined by the individual manometric measures.

The proportion of individuals displaying 'normal anal sphincter function' was determined by the 5^{th} (healthy control) percentile as described in Chapter 6.7.2 above. A sensitivity / specificity analysis was then performed under the presumption that all patients with faecal incontinence would display abnormal anal sphincter function and all healthy controls would display presumed normal anal sphincter function.

The data presented in Table 6-IV show that for description of rest, the conventional measure CAM-RA demonstrated normal anal sphincter function in 97% of healthy controls versus 26% of patients with faecal incontinence (χ^2 (1) = 27.59, p < .001). This is in line with previous published literature (McHugh and Diamant, 1987)

The highest sensitivity for detection of abnormal resting sphincter function in patients with faecal incontinence was found in the HRAM-RA with a sensitivity of 35% (χ^2 (1) = 41.73 p < .001). There appeared to be no improvement in sensitivity for detection of reduced anal function using the HRAM-RP measure (27% sensitivity, χ^2 (1) = 29.28 p < .001). All measures show good specificity (above 95%) for diagnosing normal anal sphincter function in healthy controls.

For description of squeeze, CAM-SI demonstrated 'normal anal sphincter function' in 94.1% of healthy controls versus 35.8% of patients with faecal incontinence (χ^2 (1) = 23.64, p< .001). The highest sensitivity for detection of abnormal squeeze function in patients with FI was found in the two novel profile measures. HRAM-SP-5 detected a strong significant association between group and sphincter function status (χ^2 (1) = 59.4, p< .001), with 95.3% of healthy controls demonstrating 'normal anal sphincter function' and 58.9% of FI patients demonstrating 'abnormal anal sphincter function'. This was similar to the HRAM-SP-30, which classified 95.3% of healthy controls as having 'normal anal sphincter function' and 56.8% of patients with faecal incontinence as having 'reduced anal sphincter function' (χ^2 (1) = 55.84, p< .001).

χ2 Analysis

		'accurate' classification of sphincter function		
		Healthy control (normal sphincter function)	Patient with faecal incontinence (abnormal sphincter function)	χ^2
		(Specificity)	(Sensitivity)	
Resting measures	CAM-RA (mmHg)	97%	26%	27.59***
	HRAM-RA (mmHg)	97%	35%	41.73***
	HRAM-RP (mmHg.cm.30sec)	97%	27%	29.28***
Squeeze measures	CAM-SI (mmHg)	94%	36%	23.64***
	HRAM-SI (mmHg)	95%	43%	33.38***
	HRAM-SP-5 (mmHg.cm.5sec)	95%	59%	59.35***
	HRAM-SP-30 (mmHg.cm.30sec)	95%	57%	55.84***

*** Statistically significant at the p < .0001

Table 6-IV Cross tabulation of sensitivity and specificity of manometric measures of rest and squeeze. Specificity (the proportion of correctly identified negatives) is similar across all measures. For measures of rest, the HRAM-RA measure appears to have the beset discriminative ability. For measures of squeeze the HRAM-SP-5 (highlighted) demonstrates the best result.

Therefore HRAM analysis demonstrated a 9% increase in sensitivity for detection of abnormal resting sphincter function (HRAM-RA *vs.* CA-RA) and a 23% increase in sensitivity for detecting abnormal squeeze sphincter function (HRAM-RP-5 *vs.* CAM-SI). HRAM-SP-30 demonstrated only marginally lower sensitivity than HRAM-SP-5 (2%) suggesting that further comparison of these measures is warranted.

6.7.4.2 Receiver operator curve analysis

The 'diagnostic' accuracy – in this case the discriminative ability of each measure to determine control or symptomatic status – was further explored using receiver operator characteristic (ROC) analysis.

For interpretation of anal resting pressure, inspection of the comparison ROC curves demonstrated that the conventional and HRAM average curves appeared similar in morphology, whereas the HRAM resting profile curve appeared somewhat different. At levels of low specificity, the 3 curves appear comparable, however at levels of moderate specificity there is a shift in the HRAM resting profile ROC curve suggesting an increased curve area and increased diagnostic accuracy (Figure 6-XII).

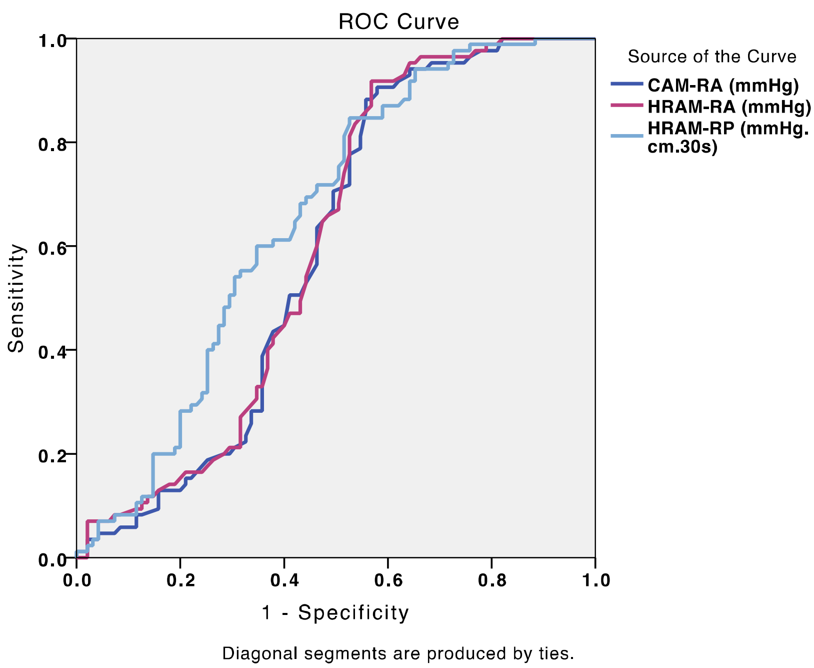

Figure 6-XII Receiver operator curves for conventional and novel HRAM resting measures. State variable = symptoms of faecal incontinence with a lower study value indicating a more positive test.

These subjective findings are reflected in a greater curve area for the novel HRAM-RP (area = .654) when compared with CAM-RA (area .592) and HRAM-RA (area = .600). This suggested marginally superior discriminative ability for the

HRAM and in particular the profile measures when compared to other measures with the HRAM-RP exhibiting a modest 6% increase in ROC curve area over the conventional CAM-RA measure.

For interpretation of squeeze, analysis of CAM-SI demonstrated a ROC area of .739 (95% CI; .667 to .810) *p*< .001. There were greater curve areas for all HRAM measures when compared with the CAM-SI (Figure 6-XIII). Differences in curve area between HRAM measures was small, however there appeared to be marginally superior discriminative ability for profile measures over the HRAM-SI measure. The best-performing measure was the HRAM-SP-5, which exhibited a 12.5% increase in area over CAM-SI (ROC area .864) (Table 6-V).

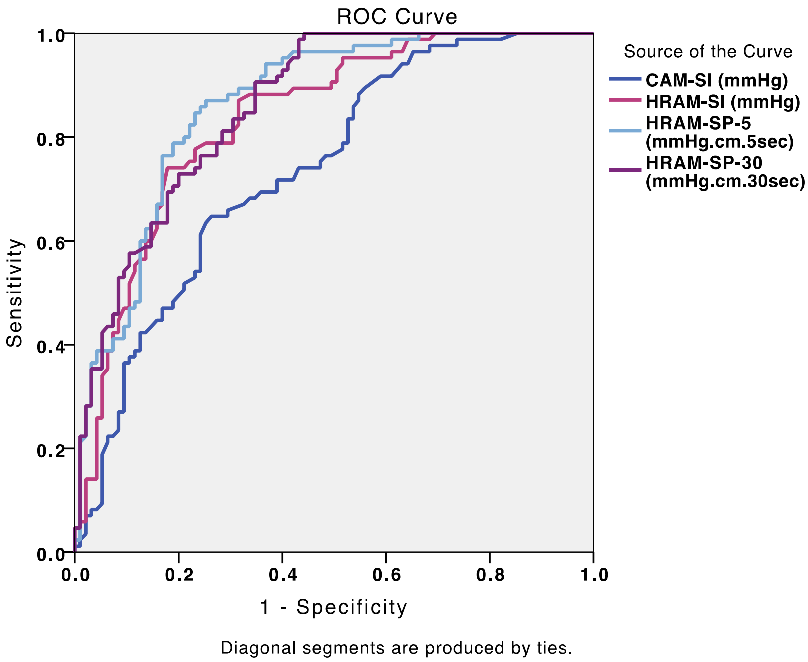

Figure 6-XIII Receiver operator curves for CAM and HRAM measures of voluntary squeeze. State variable = symptoms of faecal incontinence with a lower study value indicating a more positive test.

ROC - Area Under the Curve

		Area	SE[a]	Asymptomatic Sig.[b]	Asymptomatic Lower	95% CI Upper	Area change[c]
Resting measures	CAM-RA (mmHg)	0.592	0.04	0.34	0.51	0.68	
	HRAM-RA (mmHg)	0.6	0.04	0.021	0.52	0.69	0.008
	HRAM-RP (mmHg.cm.30sec)	0.654	0.03	< .001	0.57	0.63	0.062
Squeeze measures	CAM-SI (mmHg)	0.739	0.04	< .001	0.67	0.81	
	HRAM-SI (mmHg)	0.836	0.03	< .001	0.78	0.89	0.097
	HRAM-SP-5 (mmHg.cm.5sec)	0.864	0.03	< .001	0.81	0.92	0.125
	HRAM-SP-30 (mmHg.cm.30sec)	0.859	0.03	< .001	0.81	0.91	0.12

a. Standard Error under the nonparametric assumption
b. Null hypothesis: true area = 0.5
c. Change in ROC area from conventional squeeze increment (solid-state)
N=85 controls and N=95 patients

Table 6-V Table of ROC characteristics for CAM and HRAM measures of rest and voluntary squeeze. Novel measures demonstrate increased accuracy for prediction of state variable (faecal incontinence) as demonstrated by increased curve areas when compared with conventional measures. Area change is calculated for each measure as an increment from CAM measures. The HRAM-SP-5 exhibits the largest ROC area under the curve (highlighted blue).

6.7.4.3 ANOVA – Interaction between HRAM/CAM measures and symptom severity classification

Inspection of box and whiskers plots illustrating this visually demonstrated that, for both rest and squeeze, there appeared to be a more marked reduction in HRAM than CAM scores in those patients with severe symptoms when compared with both HV and patients with moderate symptoms of FI (Figure 6-XIV).

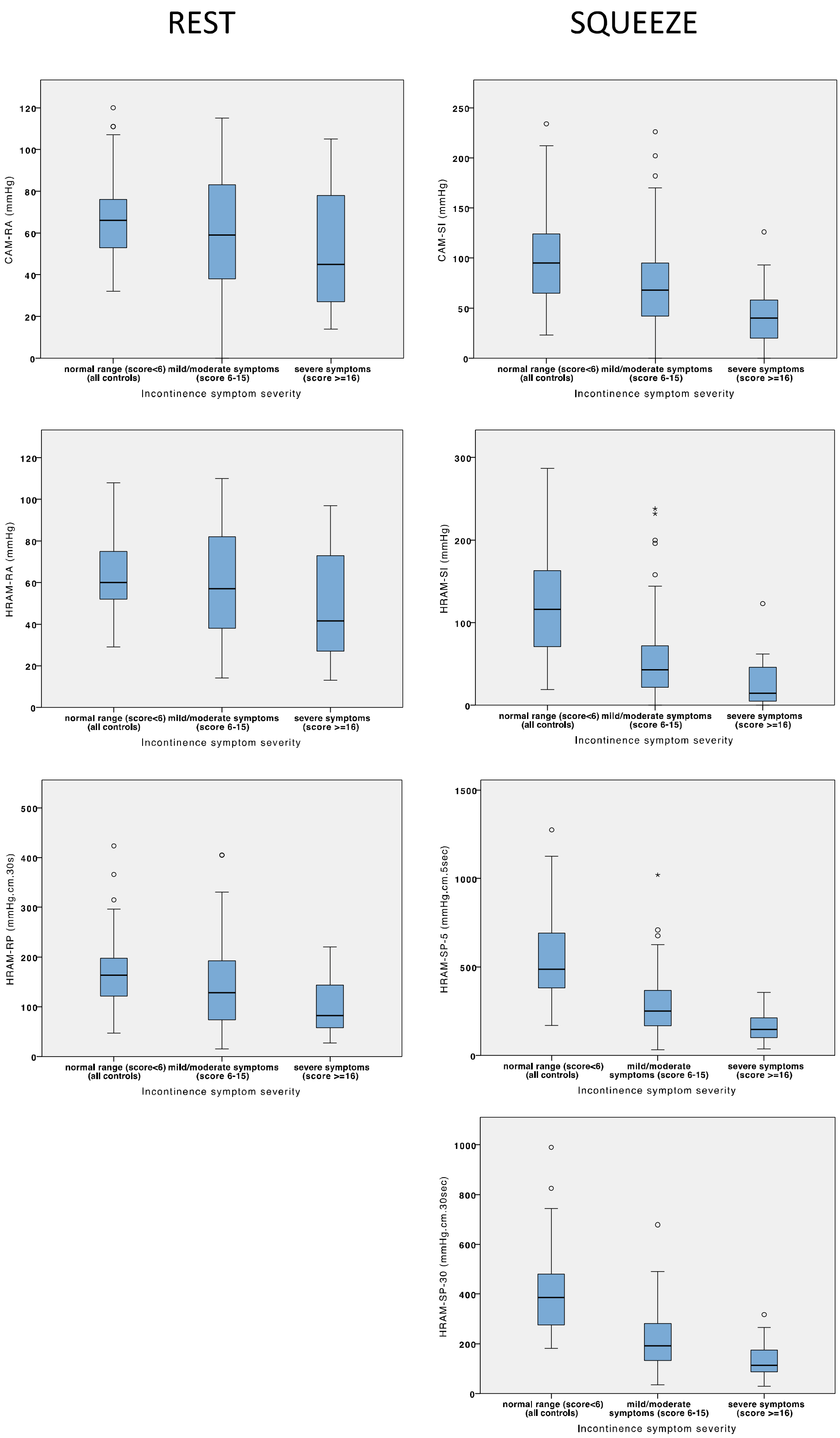

Figure 6-XIV Box and whiskers plots of CAM and HRAM measures of rest and squeeze by St Mark's symptom severity group. Normal range <6 (n=85), mild/moderate score 6 – 15 (n=73), severe score ≥ 16 (n=22).

These findings were further explored with a between-groups ANOVA to further determine the impact of symptom severity (no symptoms, mild/moderate, and severe symptoms) on CAM and HRAM measures. The findings are illustrated in Table 6-VI below.

For rest, there was a small but significant difference in all measures between groups with the largest difference seen in the HRAM-RP measures (F[2,177] = 7.07, p<.001. Although units of measurement differ, the increased significance of the HRAM-RP suggests that this instrument may be able to marginally better differentiate between mild/moderate and severe patient groups.

The greatest differences were seen for the HRAM-SP-30 and HRAM-SP-5 (F[2,177] =53.39, p<.001 and F[2,177] = 50.95, p<.001, respectively. Post hoc Tukey tests revealed that for both of these novel measures, the score was significantly lower for each increasing severity group; -130.5 mmHg.cm.5s (95% CI -241.9 to -19.15) p = .017 for HRAM-SP-5 *vs.* -88.9 mmHg.cm.30s (95% CI -167.0 to -11.0) p = .021 the HRAM-SP-30. Although units of measurement differ, the increased significance of the 5-second profile suggests that 5-second profile may better differentiate between mild/moderate and severe patient groups.

One-way ANOVA

		Mean	SD	*F*	*p*
CAM-RA (mmHg)	Normal range (score<6)	66.5	18.5	3.27	0.04
	Mild/moderate symptoms (score 6-15)	60.6	3.3		
	Severe symptoms (score >=16)	52.5	5.7		
HRAM-RA (mmHg)	Normal range (score<6)	64.624	18.0818	4.408	0.014
	Mild/moderate symptoms (score 6-15)	59.233	26.8863		
	Severe symptoms (score >=16)	48.636	25.8485		
HRAM-RP (mmHg)	Normal range (score<6)	167.6	67.6	7.07	0.001
	Mild/moderate symptoms (score 6-15)	143.3	89		
	Severe symptoms (score >=16)	101.3	56.9		
CAM-SI (mmHg)	Normal range (score<6)	100.682	44.2324	18.741	0.001
	Mild/moderate symptoms (score 6-15)	71.575	45.5936		
	Severe symptoms (score >=16)	43.091	31.4762		
HRAM-SI (mmHg)	Normal range (score<6)	121.4	64.47	38.418	0.001
	Mild/moderate symptoms (score 6-15)	56.99	53.414		
	Severe symptoms (score >=16)	24.95	29.784		
HRAM-SP-5 mmHg.cm.5sec	Normal range (score<6)	546.09	219.96	53.39	0.001
	Mild/moderate symptoms (score 6-15)	291.25	183.69		
	Severe symptoms (score >=16)	160.73	84.7		
HRAM-SP-30 mmHg.cm.30sec	Normal range (score<6)	400.38	155.41	50.95	0.001
	Mild/moderate symptoms (score 6-15)	223.87	124.81		
	Severe symptoms (score >=16)	134.88	72.34		

Table 6-VI Table of one-way ANOVA results for analysis of the effect of symptom severity on 5- and 30-second squeeze profile measures.

6.7.4.4 Partial zero order correlation analysis – correlation of squeeze results and symptom severity as determined by CAM and HRAM measures of rest and squeeze

Correlation between CAM/HRAM manometric measures and symptom severity was assessed using Pearson's correlation. An initial bivariate correlation was performed for the whole group (i.e. combining the HV and FI groups) followed by a further partial correlation analysis controlling for age and parity (coded as an ordinal variable; nulliparous = 0, parous = 1) (Table 6-VII).

Pearson's correlation with St Mark's symptom severity score

		Correlation			Partial correlation[a]		
		Co-efficient[b]	Sig.	Change[c]	Co-efficient[b]	Sig.	Change[c]
Resting measures	CAM-RA (mmHg)	-0.161	*		-0.044	n.s.	
	HRAM-RA (mmHg)	-0.19	*	-0.03	-0.084	n.s.	-0.04
	HRAM-RP (mmHg.cm.30sec)	-0.213	**	-0.05	-0.015	n.s	-0.06
Squeeze measures	CAM-SI (mmHg)	-0.403	***		-0.378	***	
	HRAM-SI (mmHg)	-0.524	***	-0.12	-0.497	***	-0.12
	HRAM-SP-5 (mmHg.cm.5 sec)	-0.573	***	-0.17	-0.538	***	-0.16
	HRAM-SP-30 (mmHg.cm.30sec)	-0.575	***	-0.17	-0.512	***	-0.13

* Statistically significant at the *p*< .05, or *** *p*< .001 level (2-tailed)

a. Partial correlation controlling for age and parity

b. Pearson's correlation co-efficient

d. Change in Pearson's correlation co-efficient from conventional squeeze increment (solid-state)

Table 6-VII Table of correlation characteristics for CAM/HRAM manometric measures for rest and squeeze with St Mark's faecal incontinence symptom severity (Vaizey) score (max=24). HRAM measures are characterized by increased negative correlation with symptom severity. Without controlling for age and parity, HRAM-SP-30 shows the greatest improvement over the conventional measure. After controlling for age and parity the HRAM-SP-5 demonstrates the greatest correlation.

For measures of rest, this demonstrated that before controlling for age and parity there was a modest negative correlation between CAM-RA and symptom severity. This reached significance r(98) = -.161, p = .031 with higher symptom severity associated with lower rest values. The negative correlation was stronger for both HRAM measures over the conventional measure however the correlations remained weak for both the HRAM-RA r[98] = -.19 p = .011) and HRAM-RP (r[98] = -.213, p <.004).

Once age and parity were controlled for, the correlation between symptom severity and values of rest (for all measures) became non significant (CAM-RA (r[98] = -.0.44, p <.533), HRAM-RA (r[98] = -.213, p <.250); HRAM-RP (r[98] = -.213, p <.151).

For measures of squeeze, there was a similar moderate negative correlation between CAM-SI and symptom severity $r(98) = -.403$, $p< .0001$. This negative correlation was markedly stronger all HRAM measures i.e. all exceeded -.5 commonly accepted as a cut-off for strong negative correlation. The most clear improvement was for the HRAM-RP-5 ($r[98] = -.573$, $p< .0001$) and the HRAM-RP-30 ($r[98] = -.575$, $p <.0001$) measures indicating that these may be the most robust indices of poor sphincter function.

Unlike for rest, when controlling for age and parity, HRAM-SP indices continued to significantly outperform the CAM measure (CAM-SI $r(94) = -.378$, $p<.0001$ *vs.* HRAM-SP-5 $r(94) = -.538$, $p< .001$).

Interestingly, the HRAM-SP-5 appeared to be less influenced by age and parity than other measures as after controlling for these covariates symptom severity explained 29% of the variation in HRAM-SP-5 scores.

These data displayed as scatter plots are shown in (Figure 6-XV) below.

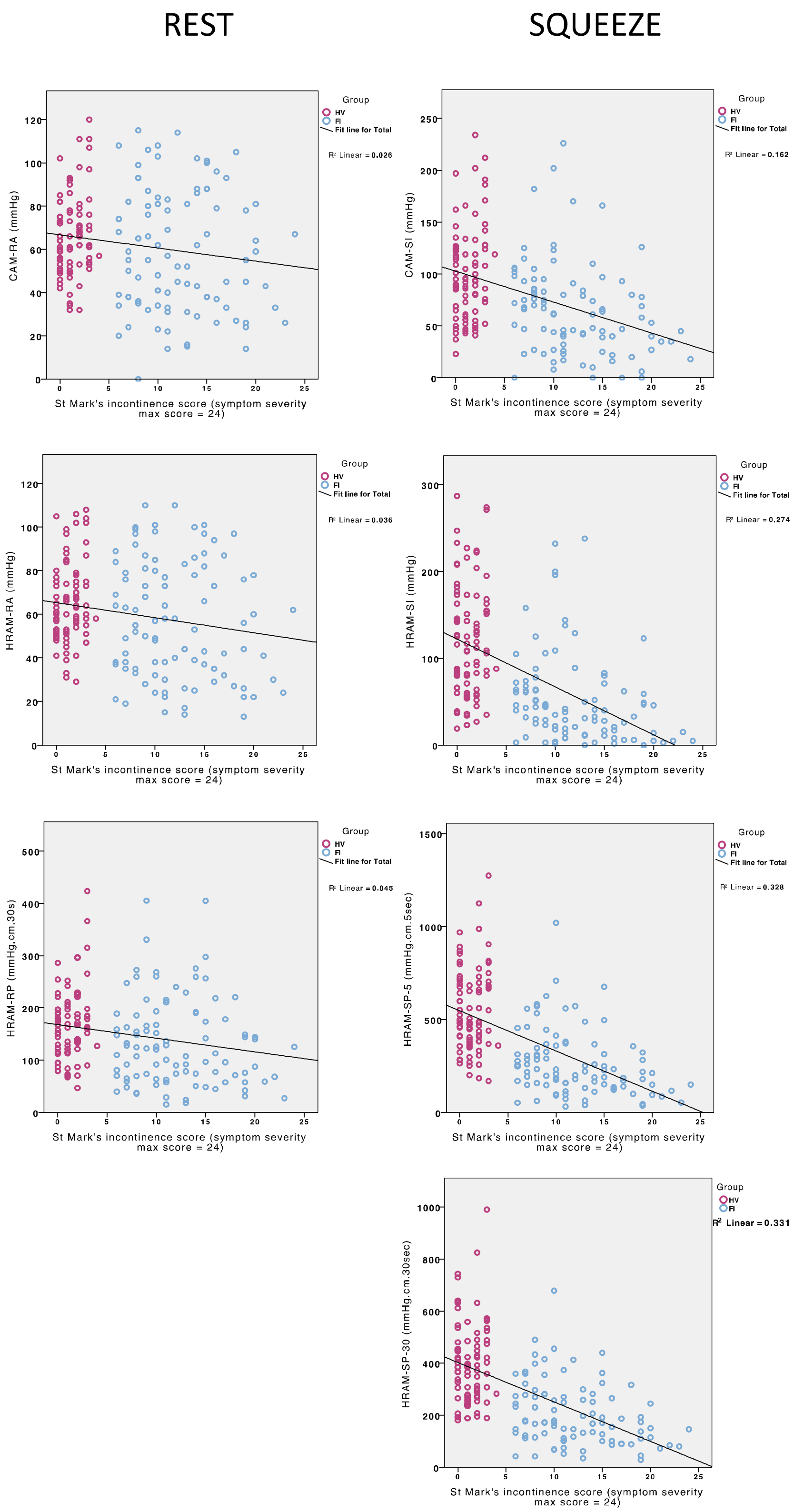

Figure 6-XV Scatter plots of squeeze value and faecal incontinence symptom severity for (a) conventional (solid-state) squeeze increment measure and (b) 5-second squeeze profile measure demonstrating the superior correlation between symptom severity and reduced squeeze function when defined by with the novel measure.

6.7.4.5 Hierarchical multiple regression – modeling of parity, age and symptom severity on squeeze results as determined by CAM and HRAM squeeze measures

Due to poor correlation between resting measurements and symptom severity (non significant after controlling for age and parity), regression modeling was further explored with squeeze measures only. A hierarchical multiple regression model was built to further evaluate the association between symptom severity and each squeeze measure after controlling for these covariates in the symptomatic FI group only (a partial analysis of the symptomatic group only was performed because endoanal ultrasound was not performed in the healthy control group).

A three-stage hierarchical regression construct was built, with the conventional and novel measures as the dependent variables, in four separate models.

In step 1 of the regression; the presumed covariates of age and parity (dummy coded: nulliparous 0, parous 1) were proposed as the independent variables, to control for their supposed influence on the outcome. In step 2, the independent variable was posited as anal sphincter status (dummy coded: normal external anal sphincter morphology 0, degenerate appearance/defect within external anal sphincter 1). In step 3, the St Mark's symptom severity score, treated as a continuous variable, was posited as another independent variable, to examine the unique contribution of symptom severity in predicting each squeeze measure, over and above the contribution of variables entered in steps 1 and 2.

Table 6-VII displays the standardized regression coefficients (β), the *t*-values, R^2 and adjusted R^2 for step 1 (nuisance covariates) step 2 (sphincter morphology) and step 3 (St Mark's symptom severity score).

Hierarchical regression														
	Step 1 (Covariates)					Step 2 (1st Predictor Variable)					Step 3 (2nd Predictor Variable)				
	Age (β)	Parity (β)	R^2	Adj. -R^2	F-ratio	Sphincter Status (β)	R^2	Adj. -R^2	R^2 Change	F-ratio	Symptom Severity (β)	R^2	Adj. -R^2	R^2 Change	F-ratio
CAM-SI (mmHg)	.013 (.116)	0.47096	0.051	0.031	2.49	-.100 (-.879)	0.059	0.028	0.008	1.91	-.430*** (-4.17)	0.212	0.177	.153***	6.05***
HRAM-SI (mmHg)	-.121 (-1.096)	0.6875	0.121	0.102	6.35**	-.173 (-1.588)	0.145	0.117	0.024	5.141	-.508*** (-5.456)	0.357	0.329	.213***	12.52***
HRAM-SP-5 (mmHg.cm.5s)	-.158 (-1.46)	0.557052	0.173	0.155	9.65***	0.50669	0.215	0.189	.042*	8.32***	-.526*** (-6.01)	0.443	0.419	.228***	17.91***
HRAM-SP-30 (mmHg.cm.30s)	-.309** (-2.99)	0.5782	0.225	0.208	13.4***	0.4264	0.259	0.235	0.034	10.6***	-.494*** (-5.79)	0.461	0.437	0.201	19.24***

* Statistically significant at the *p*< .05, ** *p*< .01 level, *** *p*< .001 level (2-tailed)

Table 6-VIII Table of standardized regression coefficients to evaluate the association between symptom severity and CAM/HRAM squeeze measures. Data pertains to patients with faecal incontinence only (N=95). Analysis demonstrates that symptom severity exerts greater influence HRAM rather than CAM measures with the HRAM-SP-30 (highlighted blue) performing the best.

For HRAM-SI, in step 1 of the model, parity (p= .045), but not age (p= .908) contributed significantly to the regression model. The combination of these covariates explained 5.1% of the variability in CAM-SI values - F(2,94) = 2.487, p=.089. The addition of the presence/absence of a sphincter abnormality only explained a further 0.8% of the variability without significantly increasing the predictive ability - F(1,91) = .773, p= .382. The final stage including symptom severity demonstrated that the individual's reported St Mark's score described a further 15.3% of the variability (F [1,90] = 17.441, p< .001). The full construct of age, parity, sphincter abnormality and symptom severity to predict conventional solid-state squeeze increment (step 3) was statistically significant R^2 = .212, F(4, 94) = 6.053, p< .0001; adjusted R^2 = .177 (final predictive ability of 17.7%)

Analysis of identical regression models for each of the HRAM squeeze measures demonstrated that in all (after controlling for nuisance covariates in the 1st step), predictive ability of the symptom severity on outcome was greater than for conventional manometry, and successively increased. Comparison of models demonstrated that the profile measures (HRAM-SP-5 and HRAM-SP-30) files were most influenced by symptom severity; with HRAM-SP-30 influenced most. In this measure, both age and parity contributed significantly in the first stage (p= .004 and p= .02 respectively) explaining 22.5% of the variability in HRAM-SP-30 scores – F(2,92) = 13.36, p= <.001. In the second stage, the addition of anal sphincter integrity led to a statistically significant increase in the R^2 of .034, F (1, 91) = 4.203, p= .043 with the presence of an underlying sphincter abnormality resulting in significantly lower 30-second squeeze profile scores. The final stage including symptom severity demonstrated that the individual's reported St Mark's score described a further 20.1% of the variability (F [1,90] = 33.63, p< .001). The full construct of age, parity, sphincter abnormality and symptom severity to predict HRAM-SP-30 (step 3) was statistically significant R^2 = .461, F(4, 94) = 19.24, p< .0001.; adjusted R^2 = .437 (final predictive ability of 43.7%).

Therefore comparison results from modelling HRAM-SP-30 and CAM-SI suggest that the influence of age, parity, sphincter abnormality and symptom severity on this novel measure is far greater with prediction of variability increasing by 26% (final predictive ability of HRAM-SP-30 model [43.7]– final predictive ability of CAM-SI [17.7]).

6.7.5 Conclusions of validation studies for HRAM squeeze measures – superiority of novel profile scores proposed

Each step of the validation demonstrated that all novel HRAM squeeze measures outperformed conventional manometry in their ability to discriminate between health and patients with faecal incontinence with novel measures displaying increased ROC curve areas and superior correlation with symptom severity which persisted after covariate control during hierarchical regression modeling. The improvement in HRAM over CAM scores for rest was present, however less marked.

Comparison between these novel measures demonstrated that in general, the HRAM-SP-5 and HRAM-SP-30 measures consistently outperformed the HRAM-SI and CAM-SI measures. However, differences between these measures were small with HRAM-SP-5 performing better during ROC and correlation analysis and HRAM-SP-30 appearing superior during hierarchical regression.

6.7.6 Validity checks for HRAM 5-second and 30-second squeeze profile measures

As the differences between HRAM-SP-5 and HRAM-SP-30 were small, a decision was made to perform further validity checks on these two instruments in order to determine the optimal measure.

6.7.6.1 Mann-Whitney U analysis – Difference in squeeze profile scores between patients with faecal incontinence grouped by external anal sphincter integrity

It would be reasonable to assume that an optimal measure of squeeze function would be able to discriminate, not only between those with symptoms of different severities, but also between those with and without external anal sphincter abnormalities. As a preliminary analysis, the HRAM-SP-5 and HRAM-SP-30 scores were compared between patients grouped according to external anal sphincter integrity (normal external anal sphincter anatomy *vs.* defect/degeneration of external anal sphincter (Figure 6-XVII).

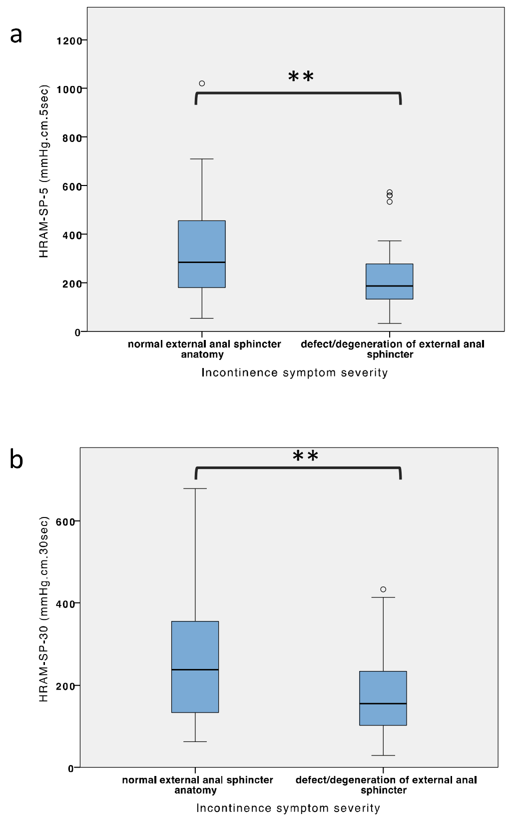

Figure 6-XVI Box and whiskers plots of (a) HRAM-SP-5 and (b) HRAM-SP-30 scores in patients with FI divided on the basis of external anal sphincter integrity. Scores for both measures appear to be reduced in those with external anal sphincter defects, though there remains considerable overlap in both measures between groups. ** Statistically significant at the *p* < .01 level.

A Mann-Whitney U analysis was performed with results confirming a significant difference in both HRAM-SP-5 and HRAM-SP-30 scores between patients with intact *vs.* damaged external anal sphincters (Table 6-IX). The marginally increased significance between groups for the 5-second measure indicated that this test might have marginally more discriminative ability than the 30-second measure.

Mann-Whitney U test descriptives

		N	Median	IQR	*p*
HRAM-SP-5 (mmHg.cm.5s)	Normal anal sphincter anatomy	38	284.2	278.3	0.003
	Defect / degenerate external anal sphincter	57	187	150.6	
HRAM-SP-30 (mmHg.cm.30s)	Normal anal sphincter anatomy	38	237.5	223.6	0.005
	Defect / degenerate external anal sphincter	47	155.4	137.8	

Table 6-IX Table of descriptives and Mann-Whitney U test results for analysis of differences in 5-second and 30-second profile scores between patients with and without external anal sphincter defects.

6.7.6.2 ANCOVA – Interaction between 5-second and 30-second squeeze profile measures and symptom severity with external anal sphincter integrity

It is well appreciated that there is an interaction effect between symptom severity and anal sphincter integrity (Bharucha et al., 2005). To examine whether differences between profile measures persist in the presence of this assumption a 2 (severity) x 2 (sphincter abnormality) between-groups ANCOVA was performed to examine the interaction of severity and sphincter abnormality on HRAM-SP-5 and HRAM-SP-30, while controlling age and parity, i.e. to examine whether the 5-second and/or 30-second measures differ by severity, and also differ by abnormality.

For the HRAM-SP-5 measure, there was a marginally significant interaction effect, $F(1,91) = 3.91$, $p = .051$; indicating that in the mild/moderate severity group, patients with normal sphincter had marginally higher HRAM-SP-5 scores (mean 383.3 mmHg.cm.5sec) than abnormal sphincter patients (mean 230.6 mmHg.cm.5sec); whereas in the severe group, HRAM-SP-5 scores were similar between those with intact (mean 161.5 mmHg.cm.5sec) and damaged external anal sphincters (mean 160.2 mmHg.cm.5sec).

This suggests that the HRAM-SP-5 score has some ability to discriminate sphincter abnormality in patients with mild-moderate symptoms, but not in those with severe symptoms as in this group, the degree of sphincter abnormality no longer influences these universally low HRAM-SP-5 scores. Figure 6-XVII illustrates the interaction effect.

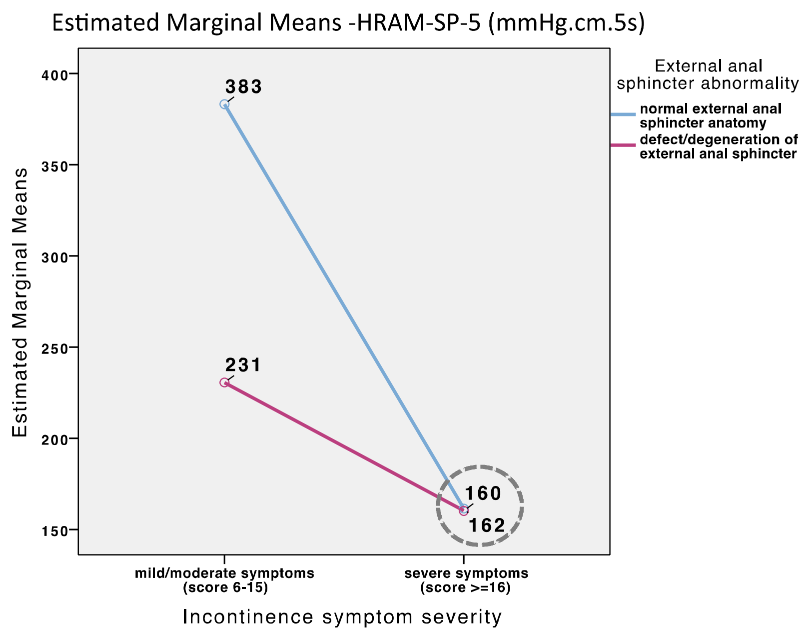

Figure 6-XVII Line graph of HRAM-SP-5 estimated marginal means in patients with intact and defective external anal sphincters according to symptom severity. This graph clearly shows that normal external anal sphincter anatomy is associated with higher HRAM-SP-5 scores in the mild/moderate symptom group, however this benefit is lost in those with severe symptoms.

For the HRAM-SP-30 measure, there was no significant interaction effect, $F(1,91) = 2.49$, $p = .117$ between symptom severity group, sphincter integrity and HRAM-SP-30 scores. Similar to the HRAM-SP-5 measure, in the mild/moderate symptom group, HRAM-SP-30 scores were higher in those with intact external anal sphincter complexes compared to those with a defective sphincter (mean 283.4 mmHg.cm.30sec *vs.* 184.6 mmHg.cm.30sec respectively).

In contrast, in the severe group (although the difference was small) HRAM-SP-30 continued to demonstrate differences between patients with and without external anal sphincter abnormalities (mean 143.4 *vs.* 129.0 respectively) (Figure 6-XVIII).

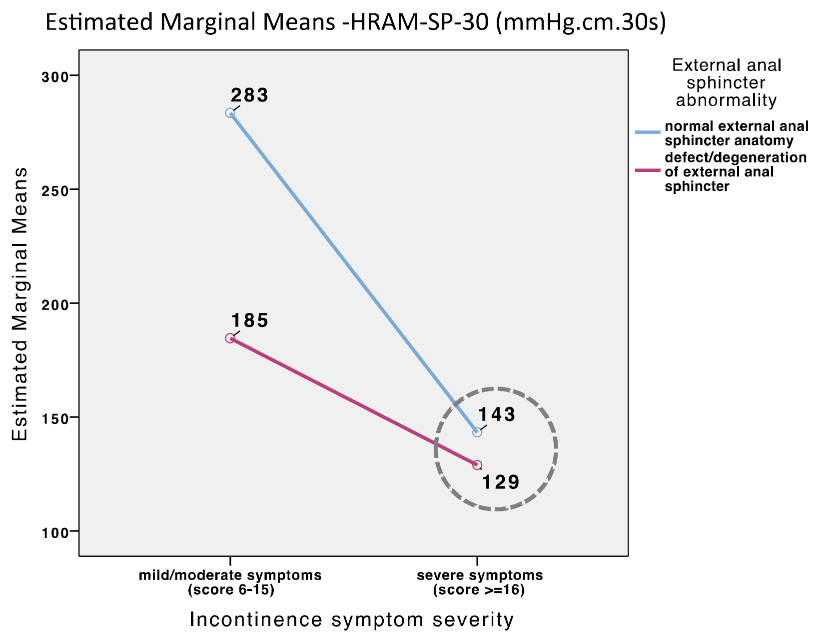

Figure 6-XVIII Line graph of estimated marginal means in patients with intact and defective external anal sphincters according to symptom severity. This graph clearly shows that normal external anal sphincter anatomy is associated with higher 5-second profile scores in the mild/moderate symptom group, however this benefit is lost in those with severe symptoms.

Therefore in contrast to the findings of the Mann-Whitney U analysis above, this analysis suggests that HRAM-SP-5 and HRAM-SP-30 may be equally good measures in patients with mild/moderate symptoms, however the HRAM-SP-30 is likely to be a superior instrument in those with severe symptoms.

6.7.6.3 Logistic regression analysis – Ability of HRAM profile measures to predict external anal sphincter integrity

To more accurately characterise the predictive ability of profile measures on external anal sphincter integrity, a binary logistic regression analysis was performed. In the patient group only, external anal sphincter anatomy status was posited as the dependent variable, with age and HRAM-SP-5 or HRAM-SP-30 score as independent variables (St Mark's symptom severity score was not included due to significant multicollinearity between this variable and profile scores as demonstrated in the section 6.7.4.5).

Logistic regression variables: HRAM-SP-5						
	β	SE	Wald	OR[a]	95% CI for OR	
					Lower	Upper
Age	0.01	0.014	0.484	1.01	0.983	1.038
HRAM-SP-5	-0.004	0.001	7.508**	0.996	0.993	0.999
Constant	0.95	0.946	1.007	2.585		

Logistic regression variables: HRAM-SP-30						
	β	SE	Wald	OR	95% CI for OR	
					Lower	Upper
Age	0.006	0.014	0.191	1.006	0.979	1.035
HRAM-SP-30	-0.006	0.002	7.059**	0.994	0.99	0.999
Constant	1.231	1.023	1.446	3.423		

note: dependent variable is external anal sphincter integrity (coded: 0 = normal external anal sphincter anatomy, 1 = defect/degeneration of external anal sphincter)
a. OR = odds ratio

Table 6-X Table of logistic regression variables for prediction of probability of external anal sphincter integrity classification according to age, parity and HRAM-SP-5 and HRAM-SP-30. **Statistically significant at the *p*< .01 level.

For the HRAM-SP-5 measure the logistic regression model was statistically significant, $\chi^2(2) = 11.10$, $p = .004$ however of poor-moderate fit (the model explained 14.9% (Nagelkerke R^2) of the variance in sphincter anatomy and correctly classified 68.4% of cases) (Table 6-X). Sensitivity was 86%, however specificity was only 42.1%, positive predictive value was 69% and negative predictive value was 66%. With each unit increase in HRAM-SP-5 score there was a 0.4% reduction in the likelihood of external anal sphincter deficiency (OR = .996 [95% CI .993 to .999], $p = .006$). Simply speaking, based on the negative β coefficient, this demonstrates that higher scores in the 5-second squeeze profile predict having normal anal sphincter anatomy (group coded 0).

Findings for the HRAM-SP-30 score were similar. The logistic regression model was statistically significant, $\chi^2(2) =9.94$, $p = .007$. The model was a poorer fit than for HRAM-SP-5 (explained 13.8% (Nagelkerke R^2) of the variance in sphincter anatomy, correctly classifying 66.3%. Sensitivity and specificity were similar (82.5 and 42.1% respectively).

These results suggest that although squeeze profile scores are moderate predictors for external anal sphincter integrity, there are likely to be other, more important factors (a likely possibility being faecal incontinence symptom severity) that contribute to the score variability.

6.7.6.4 Logistic regression analysis – Ability of HRAM squeeze profile measures to predict symptoms of faecal incontinence

Analysis to this point has focussed on the relationship between squeeze profile measures and markers of incontinence. While initial sensitivity analysis of all measures were performed using a cross tabulation analysis, a final exploration of sensitivity and specificity of squeeze profile measures was performed with a logistic regression analysis.

Binary logistic regression analysis was performed to predict the probability of accurate group classification (healthy controls vs. patients with faecal incontinence), based on HRAM-SP-5 and HRAM-SP-30 scores. Group was entered as the dependent variable; age and parity (dummy coded nulliparous = 0, parous = 1) and 5-second or 30-second squeeze profile scores were entered as independent variables (Table 6-XI).

Logistic regression variables - HRAM-SP-5						
	β	SE	Wald	OR[a]	95% CI for OR	
					Lower	Upper
Age	0.049	0.014	11.42***	1.05	1.021	1.08
Parity[b]	0.396	0.467	0.719	1.485	0.595	3.707
HRAM-SP-5	-0.007	0.001	33.99***	0.993	0.991	0.995
Constant	0.441	0.835	0.279	1.554		

Logistic regression variables - HRAM-SP-30						
	β	SE	Wald	OR[a]	95% CI for OR	
					Lower	Upper
Age	0.039	0.014	7.493***	1.039	1.011	1.068
Parity[b]	0.306	0.456	0.452	1.358	0.556	3.317
HRAM-SP-30	-0.01	0.002	32.686***	0.99	0.986	0.993
Constant	1.152	0.905	1.619	3.164		

note: dependent variable is participant group (coded: 0 =HV, 1 = patient with FI)
a. OR = odds ratio
b. Parity (dummy coded: 0 = nulliparous, 1 = parous)
*** Statistically significant at the $p < .001$ level

Table 6-XI Table of logistic regression variables for prediction of probability of group classification according to age, parity and HRAM-SP-5 above; HRAM-SP-30 below.

For the HRAM-SP-5 measure the logistic regression model was statistically significant, $\chi^2(3) = 88.88$, $p < .0005$. The model explained 52% (Nagelkerke R^2) of the variance in-group and correctly classified 77.2% of cases. Sensitivity was 77.9%, specificity was 76.5%, positive predictive value was 78.7% and negative predictive value was 75.5%. Of the three predictor variables only two were statistically significant – age and HRAM-SP-5. With each unit increase in HRAM-SP-5 score there was a 0.7% reduction in the likelihood of symptoms of faecal incontinence (OR = .993 [95% CI .991 to .995]).

For the HRAM-SP-30 measure the logistic regression model was likewise statistically significant, $\chi^2(2) = 84.71, p < .001$. The model explained 50% (Nagelkerke R^2) of the variance in group and correctly classified 76.1% of cases. Sensitivity was 77.9%, specificity was 74.1%, positive predictive value was 77.1% and negative predictive value was 75.0%. Once more, of the three predictor variables only two were statistically significant – age and HRAM-SP-30. With each unit increase in HRAM-SP-30 score there was a 1% reduction in the likelihood of symptoms of faecal incontinence (OR = .990 [95% CI .986 to .993]).

6.7.7 Summary of HRAM-SP-5 and HRAM-SP-30 sub-analyses: HRAM-SP-5 appears superior.

For interpretation of squeeze function, the above analysis has demonstrated the superiority of novel HRAM profile measures in detecting impaired anal sphincter function in patients with faecal incontinence over CAM measures. Profile measures are characterised by improved sensitivity for identification of abnormal anal sphincter function in patients with FI and show enhanced correlation with symptom severity when compared to CAM measures. Further validity analyses demonstrate the ability of HRAM squeeze profile measures to discriminate between symptom severity classification groups and also some predictive ability for the presence of external anal sphincter integrity.

The superiority of one profile measure of the other is somewhat difficult to tease apart, as results for most analyses have been similar between measures. Final outcomes from analysis for both profile measures are outlined in Table 6-XII

Summary			
		HRAM-SP-5	HRAM-SP-30
χ^2 sensitivity Classification of abnormal anal sphincter function in patients with faecal incontinence	Sensitivity	59%*	57%
ROC area Classification of abnormal anal sphincter function in patients with faecal incontinence	AUC	0.864*	0.859
Pearson's correlation coefficient Correlation with symptom severity	Co-efficient	-0.538*	-0.512
Regression final R^2 Modelling of parity, age and symptom severity	Final R^2	0.419	0.437*
ANOVA Scores according to symptom severity group	F	53.39*	50.95
ANCOVA Effect of symptom severity by sphincter integrity	Description	No discriminati ve ability in	Increased discriminative ability in those
Logistic regression Prediction of symptoms of faecal incontinence	Nagelkerke R^2	0.52*	0.5

* Indicates superior result in comparison to other profile measure

Table 6-XII Summary of findings from analyses performed within this chapter. Although differences between measures are marginal, close inspection demonstrates that the 5-second squeeze profile performs better in 5/7 analyses.

By arbitrarily counting the number of analyses in which one profile score 'wins' over the other, it could be postulated that HRAM-SP-5 is the preferred measure. However the reality is likely to be that further investigation is required across a range of patient subgroups, before such an assertion can be made.

6.7.8 Newly identified deficiency of external anal sphincter function – a closer analysis of those previously 'misdiagnosed'

Adoption of the new HRAM-SP-5 measure for description of squeeze identifies a previously unrecognized subgroup of patients, who previously (using CAM measures) were reported to have normal anal sphincter function. It is likely that management strategies for this group may now differ on the basis of newly diagnosed voluntary sphincteric compromise therefore further characterization of this patient group was performed.

6.7.8.1 Agreement between existing and novel squeeze tests

A cross tabulation of results in patients with faecal incontinence was performed in order to determine agreement between the existing reference test (CAM-SI) and the novel measure (HRAM-SP-5). Inspection of the crosstabs demonstrates that 25/61 patients classified with the conventional measure as having normal anal sphincter function were demonstrated to have reduced function using the HRAM-SP-5 measure (26% of the cohort as a whole). In addition 3/24 of those classified with the conventional measure as having reduced anal sphincter function were demonstrated to have normal function using HRAM-SP-5 (3% of the cohort as a whole) (Table 6-XIII).

Kappa analysis demonstrated poor agreement between the tests (Kappa = -.135 (SE = .025), p<.001) with a positive percent agreement of 40.9% and a negative percent agreement of 91.1%.

Cross tabulation

		CAM-SI		
		Normal result	Reduced function	Total
HRAM-SP-5	Normal result	36	3	39
	Reduced function	25	31	56
	Total	61	34	95

Table 6-XIII Cross tabulation of sphincter function in patients with faecal incontinence (N=95) as reported by CAM-SI (current accepted best practice measure) and HRAM-SP-5 (newly proposed measure)

6.7.8.2 *Demographics of newly identified patients with reduced squeeze sphincter function*

Using the HRAM-SP-5 measure, twenty-five patients who would have been reported as having normal anal sphincter function using CAM-SI were identified as having impaired sphincter function. Analysis of demographics demonstrated that characteristics of this group appear similar to the incontinent group as a whole. Median age of this group was 60 (range 50-81) and St Mark's symptom severity score 12 (6-23). Twenty-one were parous and 14/15 had evidence of an external anal sphincter defect.

Dot plots of (a) HRAM-SP-5 and (b) CAM-SI by test agreement category confirmed that the 'newly identified' group consisted of patients with conventional scores towards the lower limit of normal (Figure 6-XIX). This likely represents a group with somewhat impaired function, to a degree not great enough to distinguish using the conventional measure.

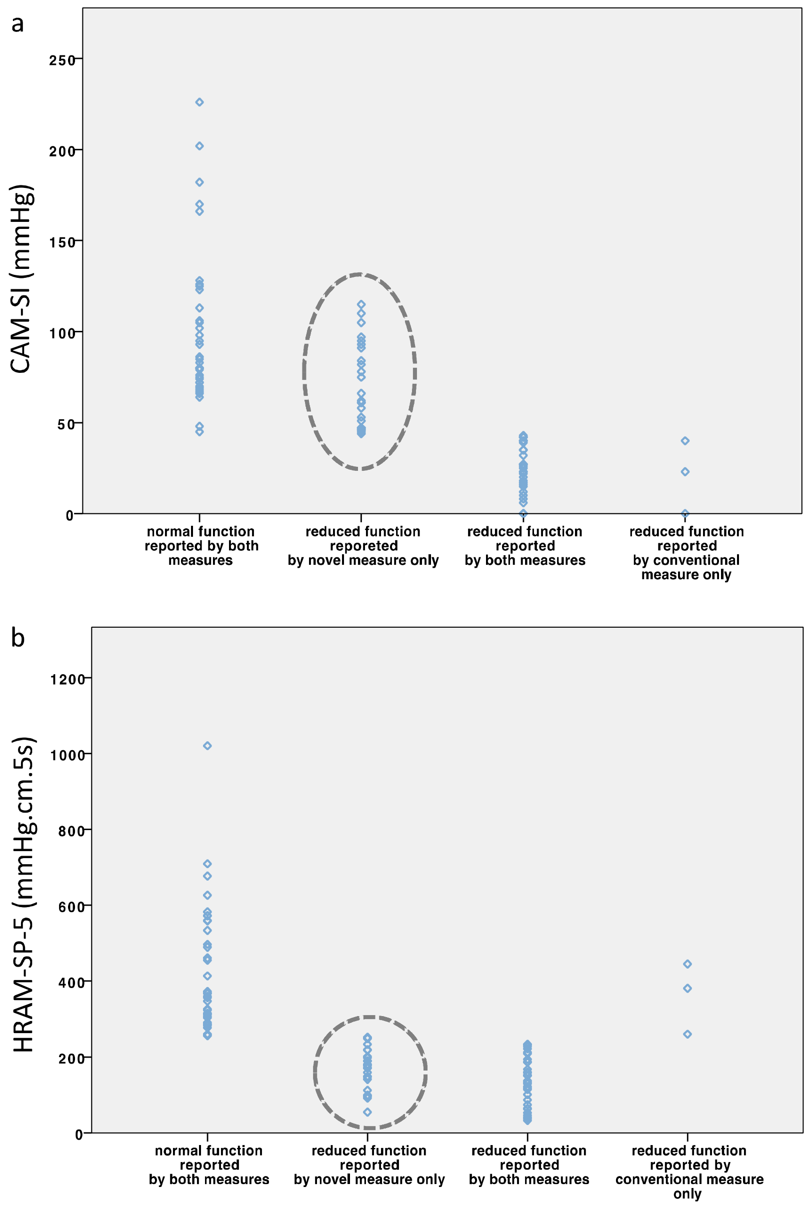

Figure 6-XIX Dot plots of (a) HRAM-SP-5 and (b) CAM-SI scores in patients with faecal incontinence categorized by test agreement category. The newly identified group with impaired function as determined by the novel measure is circled in grey in both graphs.

6.7.8.3 Agreement between existing and novel rest tests

Similar to 6.7.8.3 for squeeze above, a cross tabulation results for describing resting pressure in patients with faecal incontinence was performed in order to determine agreement between the existing reference test (CAM-RA) and the novel measure (HRAM-RA) (Table 6-XIV).

Cross tabulation				
		CAM-RA		
		Normal result	Reduced function	Total
HRAM-RP	Normal result	61	1	62
	Reduced function	9	24	33
	Total	70	25	95

Table 6-XIV Cross tabulation of resting sphincter function in patients with faecal incontinence (N=95) as reported by CAM-RA (current accepted best practice measure) and HRAM-RA(newly proposed measure)

Inspection of the crosstabs demonstrates that 9/70 patients classified with CAM-RA as having normal anal sphincter function were demonstrated to have reduced function using the HRAM-RP measure (9% of the cohort as a whole). In addition 1/25 of those classified with the conventional measure as having reduced anal sphincter function were demonstrated to have normal function using the HRAM-RP measure (1% of the cohort as a whole). Therefore it can be assumed that although the improvement in identification of cases is not as marked as for the HRAM-SP-5 measure, the HRAM-RP is marginally improved over existing CAM measures.

6.8 Discussion

This chapter has presented a novel method for analysis of voluntary and involuntary anal sphincter function using HRAM by defining a new profile measure to describe rest and squeeze function incorporating average pressure increases throughout the whole anal canal over time. This measure is akin to (an inspired by) the distal contractile interval, which is now routinely used to describe contractile vigor within the esophagus (Ghosh et al., 2006b).

Applying this measure to healthy volunteers and patients with FI (the largest HRAM sample of both to date), this chapter has demonstrated improved diagnostic accuracy in discriminating health status with a 9% increase in sensitivity for detection of abnormal resting sphincter function (HRAM-RA *vs.* CA-RA) and a 23% increase in sensitivity for detecting abnormal squeeze sphincter function (HRAM-RP-5 *vs.* CAM-SI).

In patients with FI, this measure was also more responsive to changes in patient phenotype in respect of its association with increasing symptom severity and anal sphincter defects. Indeed, regression modeling incorporating age, parity, sphincter abnormality and symptom severity to predict HRAM-SP-5 scores had a final predictive ability of 41.9%)

Finally we have been able to characterize a new and significant group of patients (9/95 [9.4%] for rest and 25/95 [26.3%] for squeeze) with abnormal function who using previous manometric measures might have been denied further investigation on the basis of a normal test result.

The profile form of analysis appears in all forms to be a discriminative manometric measure of anal sphincter function. Analyses suggest that for squeeze, the HRAM-SP-5 is a better discriminator overall, however the author proposes the use of both measures pending further investigation as the HRAM-SP-30 has increased ability to categorize functional ability in symptomatically severe patients.

Similar to application of the profile measure to analysis of squeeze, during investigation of basal anal tone at rest, the HRAM-RA demonstrates improved sensitivity for identification of abnormal anal sphincter function in patients with faecal incontinence. There is however no real correlation with symptom severity when controlling for known confounders (age and parity).

6.8.1 Methodological limitations

The author acknowledges a number of limitations within this study. First, is that the sample size was based on feasibility and not on a prior calculation of the sample size based on the differences between binary groups as similar pilot data was not available. Despite this, the numbers in this study are comparable to similar published and widely circulated studies of novel manometric parameters (Fox et al., 2004, Ghosh et al., 2006b, Ratuapli et al., 2012).

Secondly, for ease of analysis due to functional differences in anal sphincter function between healthy males and females (Poos et al., 1986, McHugh and Diamant, 1987, Akervall et al., 1990), this study included data from female participants only. This significantly limits the application of assumptions to male patients, as it is reasonable to assume that some associations found within these analyses will differ when applied to a male cohort. In particular it is likely that correlation of HRAM-SP-5 and symptom severity in males will be weaker. A recent study of 160 male patients with a primary presenting complaint of faecal incontinence reported that only 34% demonstrated a functional sphincteric deficiency on conventional manometry (Burgell et al., 2010) far less than would be expected from a female cohort (Bharucha et al., 2005). It could be postulated that the increased discriminative ability of the HRAM-SP-5 measure may be advantageous when applied to male patients, however this hypothesis requires further investigation.

Thirdly it was assumed that all healthy participants possessed normal anal sphincter function. Seventy-five of the 135 healthy volunteers were parous and the deleterious effect of vaginal delivery on sphincter function has been well documented (Fynes et al., 1999, Chaliha et al., 2007). There was unfortunately no formal assessment of sphincter anatomy with endoanal ultrasound, and if extrapolated from previous studies, it could be assumed that between 29-38% (Sultan et al., 1993a, Belmonte Montes et al., 1999, Fynes et al., 1999, Chaliha et al., 2001) of the healthy parous volunteers included in this study have a degree of damage to the external sphincter. Analysis of traditional measures of anal squeeze function in health within previous chapters of this thesis highlights this 'asymptomatic decline in sphincter function'. However, the fact remains that these volunteers report normal continence, and demonstrate normal symptom severity scores. The question of whether a healthy volunteer can display 'abnormal sphincter function' whilst asymptomatic is a philosophical question that will be addressed in later chapters of this thesis.

With particular reference to rest, a notable limitation is the difference in age between the healthy volunteer and patient groups. A large body of historical data suggest that anal resting pressure may decrease with age (Enck et al., 1989, Akervall et al., 1990, Felt-Bersma et al., 1991, Cali et al., 1992, Noelting et al., 2012). For this reason it could be argued that differences seen in the patient group may be exaggerated in this study (as they were significantly older than the healthy volunteer cohort).

Due to this concern, analysis of resting pressure scores in healthy volunteers demonstrates that in this particular study no correlation was demonstrated between anal resting pressure and age as measured by either the conventional or HRAM resting profile measure (Partial Pearson's correlation controlling for parity – conventional anal rest $r(82) = .114$, $p = .31$; HRAM-RP $r(82) = .025$, $p = .82$). Where possible, attempts were made to correct for this (for example during Pearson's correlation analyses) however results in this context should be interpreted with caution.

Finally, is the assumption that in the patient group the symptoms of faecal incontinence in all patients are directly related to sphincteric compromise. It is well appreciated that patients with faecal incontinence do not have homogenous underlying pathophysiologies. As faecal continence is a result of coordinated sensory and motor function of the colon and anorectum it is unlikely that any single method of assessment would have inherent generalizability. Although squeeze profile measures were found to correlate well with symptom severity in this study, it is likely that some of the unexplained variability is secondary to other pathophysiological mechanisms.

6.8.2 Implications of the present study

As the new measure may only be calculated with a HRAM system, this study provides the first evidence of superiority of HRAM over conventional anal manometry. Such findings in the upper GI tract have revolutionized the practice of oesophageal manometry and have lead to the development of an internationally recognized standard in manometric practice (Kahrilas et al., 2008).

The addition of this technique of analysis to manometric studies has a number of potential implications for clinical practice. Identification of reduced sphincter function in a larger proportion of patients with faecal incontinence is likely to influence diagnosis and treatment stratification. Patients who were previously denied treatments aimed at improving residual sphincter function (e.g. biofeedback) might now, on the basis of this investigation, be eligible for intervention. This has the potential for improving outcomes in those whose management may previously have been misdirected. Prospective studies are required to identify if squeeze profile measures can accurately act as a biomarker for treatment stratification.

In addition, the increased discriminative ability of profile measures may well prove useful during application to examination of changes in sphincter function following intervention e.g. sphincter repair, as a more sensitive measure may demonstrate functional differences that have previously been unidentified during the use of conventional measures. This has significant potential use for treatment monitoring and may act as an objective marker in a field, which is notorious for treatments that harbor a significant placebo effect.

Ultimately, prospective studies with larger samples sizes are required to further establish the usefulness and correct application of this novel measure within clinical practice.

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Chapter 7

7 Prolonged studies of anorectal function using high resolution anal manometry in healthy volunteers and patients with faecal incontinence: characteristics of transient anal sphincter relaxations

7.1 Rationale

7.1.1 Role of anal sensorimotor function in the maintenance of continence

It is well recognized that the maintenance of continence is a result of the coordinated sensorimotor activity of the colon, rectum and anus. The aetiology of Faecal incontinence (FI), is usually multifactorial (in 80% of cases) and may result from dysfunction emanating from any one part or more parts of this functional unit (Rao and Patel, 1997).

In particular, the importance of adequate anorectal sensory function is well appreciated (Scott and Gladman, 2008) and the anal canal is richly innervated with a variety of free and organized nerve cells thought to respond to changes in temperature, touch, pressure and friction (Duthie and Gairns, 1960). Anal sensitivity to both electrical (Felt-Bersma et al., 1997) and thermal (Miller et al., 1988b) stimulation has been shown to be reduced in a number of functional bowel disorders including faecal incontinence (Felt-Bersma et al., 1997), chronic constipation (Felt-Bersma et al., 1997, Vasudevan et al., 2007), hemorrhoids (Felt-Bersma et al., 1997), perineal descent (Miller et al., 1989a), diabetes mellitus (Speakman and Kamm, 1993) and mucosal prolapse (Felt-Bersma et al., 1997). Despite this, the exact role of anal sensation in the maintenance of continence is not fully understood (Gladman et al., 2009).

Nevertheless, assessment of anal and rectal sensation remain part of routine of anorectal physiological investigation in many specialist units (Azpiroz et al., 2002). In addition, investigation of the physiological basis of continence continues to be an important consideration as there is continued evolution of novel treatments available to manage anorectal disorders which are thought to act through modulation of sensory function (such as sacral nerve stimulation [SNS] and percutaneous tibial nerve stimulation [PTNS]) (Norton et al., 2007, Knowles et al., 2012, Thin et al., 2013, Carrington et al., 2014b).

7.1.2 Anal sampling / transient anal sphincter relaxations (TASRs)

The concept of anal sampling was first proposed in a study of rectal and anal sensory function in 1963. This manuscript by Duthie and Bennett demonstrated that during periods of rectal distension, proximal anal canal relaxation occurred to an extent that allowed pressures within the anal 'sensory zone' to equalize with rectal pressures (Cheeney et al., 2012).

This lead to the theory of 'anal sampling' - considered to be an involuntary reflex process during which the anus examines rectal contents allowing discrimination between flatus and stool (Scott and Gladman, 2008). Spontaneous falls in anal sphincter pressure are reported to occur at rest approximately 7 times per hour and are associated with the passage of flatus. A proportion of these are thought to be consciously perceived (approximately 40%) (Miller et al., 1988c).

Experimental provocation of this phenomenon is commonly performed during routine anorectal physiology assessment by manometric assessment of anal tone during inflation of a balloon within the rectum (known as the recto-anal inhibitory reflex [RAIR]) (Rao et al., 2002). There is evidence of alteration in RAIR characteristics in patients with FI (Sangwan and Solla, 1998, Kaur et al., 2002, Jung et al., 2014), however there is little data examining the association between sampling characteristics, sensory perception and symptoms of disordered defaecation.

Nevertheless, it is generally accepted that anal sampling is likely to play an important role in the maintenance of faecal continence, due to the demonstration that differences exist in the frequency of these events between patients with faecal incontinence and continent individuals (Miller et al., 1988c, Miller et al., 1988a, Farouk et al., 1994).

Despite the assumed importance of the integrity of this reflex, to the authors' knowledge only a single study investigating anal sampling over a prolonged period *per se* exists. This pilot study demonstrated spontaneous drops in anal sphincter pressure without conscious recognition (Miller et al., 1988a). The technology used to measure anal pressure changes (a microtransducer manometer with only 3 measurement channels) is now significantly outdated and considered obsolete.

An important point to emphasize is that, to date, there has been no confirmation of the passage of rectal contents through to the anus during these relaxation episodes; therefore the use of the term "sampling" is somewhat speculative. For this reason, thereafter, the author will refer to these events as transient anal sphincter relaxations (TASRs).

7.1.3 Utility of high resolution anal manometry

More detailed examination of anorectal events is now possible due to the introduction of high-resolution anal manometry (HRAM). This method provides significantly more accurate measure of anal pressures, both radially and longitudinally than traditional manometry (Jones et al., 2007). Data from Chapters 6 and 7 of this thesis and previously published data from our group has established the utility of this technique and has demonstrated that novel methods of HRAM analysis have increased in sensitivity for detection of abnormal sphincter function in FI over conventional measures (Ambartsumyan et al., 2013, Carrington et al., 2014a).

HRAM uses an increased number of more closely spaced microtransducers than conventional manometry, greatly enhancing spatial resolution. It has the ability to measure pressure changes circumferentially and software allows interpolation between adjacent microtransducers providing the operator with more intuitive topographical plots of intraluminal pressure events relative to time and location. To date, there are no studies that have examined prolonged anorectal function using this technique.

7.2 Aims

The aim of this study were:

- To perform the first prolonged examination of anorectal motor function using HRAM
- To examine characterise TASRs morphological characteristics in health and in faecal incontinence
- To examine the effects of a standardized high fat meal on TASR frequency and characteristics in health and faecal incontinence
- To explore association of events with conscious perception, in particular to explore the effects of abnormal rectoanal sensation in patients with faecal incontinence on TASR perception

7.3 Methods

7.3.1 Recruitment – healthy volunteers

Twenty-seven healthy, male and female subjects were recruited at Barts and the London School of Medicine and Dentistry, London. Ethical approval was granted by the Queen Mary University Research Ethics Committee (ref QMREC2012/05).

The following exclusion criteria were applied:

6. Symptoms of defaecatory dysfunction, particularly those of faecal incontinence or constipation (as assessed by modified Vaizey score [<5]

(Vaizey et al., 1999) and Cleveland Clinic constipation score [<8] (Agachan et al., 1996) respectively);

7. History of previous anorectal surgery;
8. Significant GI disease
9. Use of medications that may affect anorectal function;
10. Inability to provide informed consent;

7.3.2 Recruitment – patients with FI

The FI group consisted of 10 female patients with a primary presenting complaint of FI. These patients were recruited at Barts and the London School of Medicine and Dentistry, London. Ethical approval was granted by the National Research Ethics Service (ReDA ref 008869 QM, REC ref 13/SC/0087). The following exclusion criteria were applied to this group:

- Inability to provide informed consent for the research study
- Active treatment for symptoms of faecal incontinence (excluding medications such as loperamide and codeine phosphate)
- Neurological diseases such as diabetic neuropathy, multiple sclerosis and Parkinson's disease
- Congenital anorectal anomalies or absence of native rectum due to surgery
- Present evidence of external full thickness rectal prolapse
- Previous rectal surgery (rectopexy/resection) performed <12 months ago
- Stoma in situ
- Chronic bowel diseases such as inflammatory bowel disease, chronic uncontrolled diarrhoea
- Pregnancy or intention to become pregnant.

7.3.3 Experimental methods

Participants were given a study information leaflet at least 48 hours prior to attendance and asked to sign a consent form prior to enrolment in the study. All subjects attended starved for 2 hours prior to arrival and encouraged to open their bowels before commencement of the experiment.

The study began with a focused clinical history of anorectal function and general health. Basic demographics including parity in females were recorded. The modified St Marks incontinence score (Vaizey et al., 1999), PAC-SYM score (Slappendel et al., 2006) and Cleveland Clinic Constipation score (Agachan et al., 1996) were completed.

The participant was placed in the left lateral position and a clinical examination of the anorectum including a digital rectal examination (DRE) was performed. Rectal sensation to balloon distension was performed assessing first constant sensation (FCS), defaecatory desire volume (DDV) and maximum tolerated volume (MTV). Anal sensation to electrical stimulation was assessed at 1, 2 and 3 cm from the anal verge.

The solid-state HRAM catheter was positioned in the anal canal and placed with the 2nd most distal sensor at the level of the anal verge allowing the reference sensor to be 2 cm from the anal verge (Figure 7-I). The catheter was then secured in position using adhesive tape to prevent movement during the experiment.

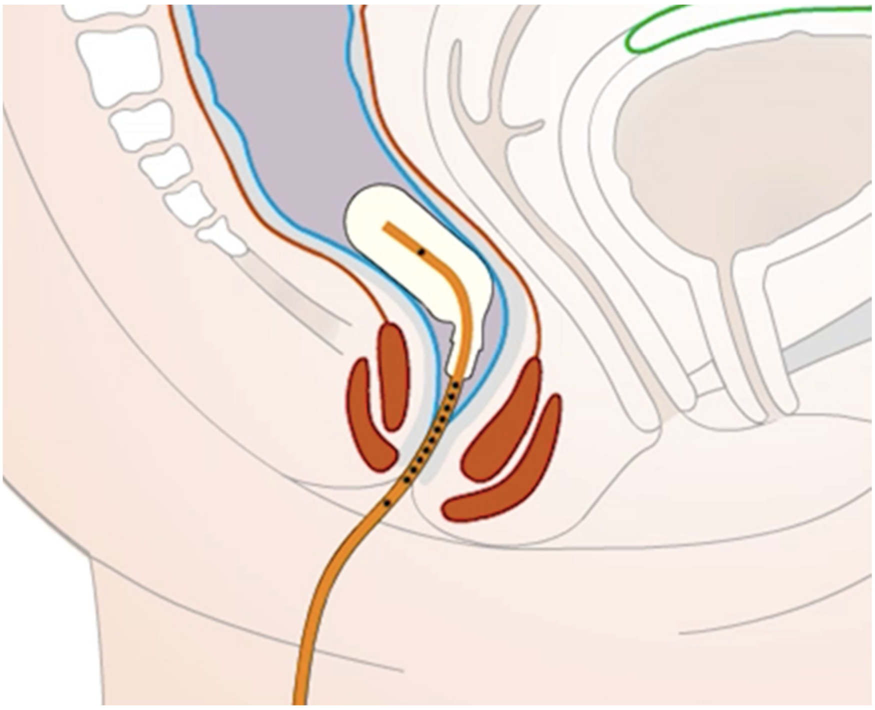
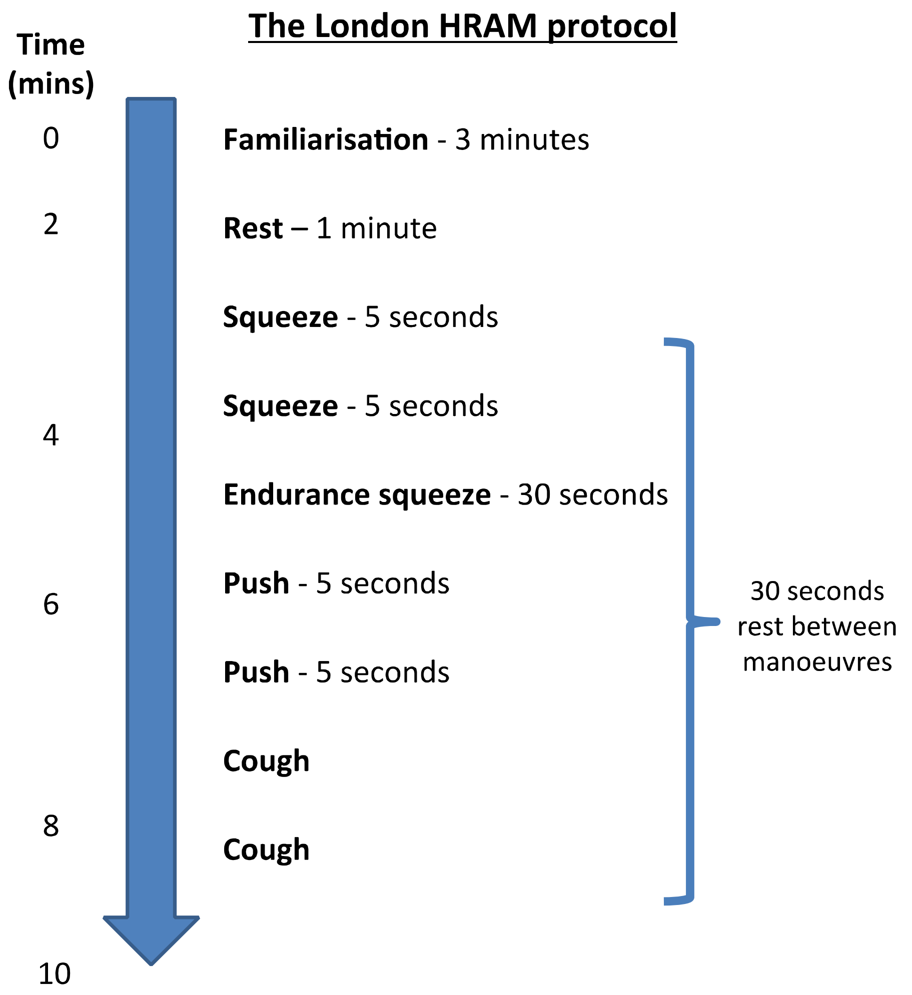


Figure 7-I Schematic demonstrating positioning of the HRAM catheter. The 2nd most distal sensor is positioned so that it is just visible at the level of the anal verge.

Routine baseline anorectal manometry was performed to assess sphincteric function as previously described in Chapters 4 and 5 of this thesis (Carrington et al., 2014a) (Figure 7-II).



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of 45 minutes (termed the pre-prandial resting period). At the end of the pre-prandial resting period the subject was given 20 minutes to consume a standard high fat meal (beef lasagne, chocolate éclair and carton of apple juice: total 907 kcal, 48.6g fat, 48.3g carbohydrate). Anorectal pressures were then measured for a further 45 minutes. This stage was termed the post-prandial resting period. The protocol is depicted in Figure 7-III below.

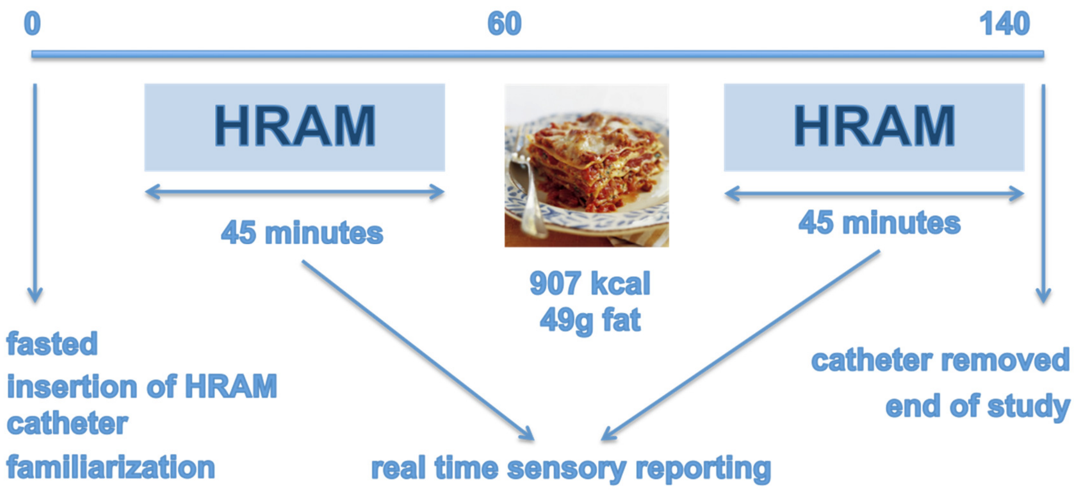

Figure 7-III Schematic of prolonged HRAM study protocol.

During pre-prandial and post-prandial resting periods, participants were asked to report (in real time) all gastrointestinal and rectoanal sensations. These were categorised as: hunger; urge to pass wind; urge to pass stool; stomach rumbling; belching or the urge to belch; abdominal pain; passing wind; passing stool. The intensity of each of these sensations was rated on a standard 10cm visual analogue scale (VAS) (0 = no feeling at all; 10 = strongest feeling imaginable).

At the end of the post-prandial resting period, the catheter position was noted prior to removal to confirm that no displacement had occurred during the recording period.

7.3.4 Experimental techniques

7.3.4.1 High resolution anal manometry

HRAM was performed using a solid-state catheter (UniTip: UniSensor AG, Switzerland), of 12F external diameter, incorporating 12 microtransducers, each of which measured circumferential pressure by means of a unidirectional pressure sensor embedded within silicone gel. Ten of these sensors were spaced 0.8 cm apart, spanning 7.2 cm. The most proximal microtransducer was located within a non-latex balloon 3.3 cm proximal to these. The most distal sensor (located 2 cm below the most distal of the central 10 sensors) was used as an external reference.

Before every study, the catheter was immersed in tepid water for at least 3 minutes to pre-wet the sensors. Sensors were then zero-ed to atmospheric pressure under 1cm of water according to manufacturers guidelines. Data acquisition, online visualization and signal processing were performed using a commercially available manometric system (Solar GI HRM v9.1, Medical Measurement Systems (MMS), Enschede, Netherlands).

7.3.4.2 Rectal sensation to balloon distension

Studies were performed using a latex balloon mounted on a Foley catheter. The tip of the balloon was placed within the rectum at 10 cm from the anal verge. Inflation was with air at a rate of 1 ml/sec. Normal values were as described previously in 92 healthy volunteers (Mohammed et al., 2010b): first constant sensation 20-110mls females, 15-150mls males; desire to defaecate 40-200mls females, 40-190mls males; maximum tolerated volume 75-290mls females, 75-325mls males.

7.3.4.3 Anal sensation to electrical stimulation

Assessment of anal sensation to electrical stimulation was performed using a bipolar stimulating catheter of 5mm external diameter, incorporating 2 stimulating electodes each of 1mm width, with an inter-electrode distance of 1cm (Gaeltech, Skye, UK). A ground electrode was placed around the wrist and the catheter inserted into the anal canal with the distal electrode 1cm from the anal verge. Anal sensitivity was determined using a square wave electrical current of 0.1ms pulse width, 10Hz frequency. The intensity of stimulation was increased gradually from 0.0 to a maximum of 30.0mA in increments of 0.2mA at a rate of 1mA per second until sensory threshold was reached. Sensory thresholds were measured 3 times and the mean value recorded. A normal upper limit of 10.4mA using this technique has been described previously (Zbar et al., 1999b) and was used for this study.

7.4 Data analysis

7.4.1 Anal sphincter function

Assessment of baseline anal sphincter function was determined by analysis of the HRAM average anal resting pressure, the 30-second anal resting profile (as described in Chapter 7), the HRAM average incremental squeeze pressure and the 5-second anal squeeze profile (as described in Chapter 6) (Ambartsumyan et al., 2013). The following definitions were used:

Functional anal canal length (FACL)

This was defined as the length of anal canal (cm) in which pressure exceeded rectal pressure by >5 mmHg.

Average anal resting pressure

This was defined as the average maximum pressure (mmHg) over the FACL during the 1-minute period of rest.

30-second anal resting profile

This was defined as the mean pressure measured from all sensors within the anal canal (mmHg) multiplied by the FACL (cm) during the 30-second period of rest and expressed in units of mmHg.cm.30secs.

Maximum incremental anal squeeze pressure

This was defined as the maximum-recorded pressure (mmHg) at any point during voluntary squeeze, minus the mean maximum resting pressure prior to the manoeuvre (over 5 seconds).

5-second anal squeeze profile

This was defined as the mean pressure measured from all sensors within the anal canal (mmHg) during the squeeze manoeuvre multiplied by the FACL in cm during the 5-second period of squeeze and expressed in units of mmHg.cm.5secs.

7.4.2 Transient anal sphincter relaxation – definition

Although anal sphincter relaxations have been described, the existing definitions pertain to conventional (low resolution) manometry. The most accepted definition is that reported by Duthie who described that proximal anal canal relaxation occurred to an extent that allowed pressures within the anal 'sensory zone' to equalize with rectal pressures (Cheeney et al., 2012).

There is currently no specific accepted definition of a transient anal sphincter relaxation as defined by HRAM. For this reason, a TASR was defined as a sporadic event characterized by equalization of anal and rectal pressures including >20% of the anal canal.

7.4.3 Transient anal sphincter relaxation – characteristics

The following data of TASR characteristics were collected:

Morphological characteristics

- TASR duration – defined as the period of time (seconds) of equalization of anal and rectal pressures in the proximal anal canal
- TASR depth – defined as the length of the anal canal (cm) in which there was equalization of anal and rectal pressures
- Percentage TASR depth – defined as the percentage depth of the anal canal involved during the TASR

Pre-TASR pressures

- Pre-TASR rectal pressure – defined as the average value (mmHg) recorded from all sensors within the rectum during the 5 seconds preceding TASR onset
- Pre-TASR anal pressure – defined as the average value recorded from all sensors within the anal canal (mmHg) during the 5 seconds preceding TASR onset

TASR pressures

- TASR rectal pressure – defined as the average value recorded from all sensors within the anal canal (mmHg) during the TASR nadir
- TASR anal pressure - defined as the average value recorded from all sensors within the anal canal (mmHg) during TASR nadir
- TASR anal minimum pressure - defined as the minimum value recorded from all sensors within the anal canal (mmHg) during TASR nadir

TASR pressure changes

- Rectal pressure change – defined as Pre-TASR rectal pressure minus TASR rectal pressure (mmHg)
- % Rectal pressure change – defined as

$$\frac{\text{TASR rectal pressure}}{\text{Pre-TASR rectal pressure}} \times 100$$

- Anal pressure change – defined as Pre-TASR anal pressure minus TASR anal pressure (mmHg)
- % Anal pressure change – defined as

$$\frac{\text{TASR anal pressure}}{\text{Pre-TASR anal pressure}} \times 100$$

7.5 Statistical analysis

Variables were summarized using number of observations, mean, lower and upper 95% confidence intervals, standard deviation, median, interquartile range, minimum, maximum and skewness.

To assess the impact of meal ingestion, age, sex and parity on these variables, Mann Whitney U tests were employed. Though due to the small sample size of this pilot study (N = 27, 8 males, 19 females) the statistical analyses are underpowered, therefore not all statistically significant results may be detected.

To assess the differences between the HV and FI groups, initial Mann Whitney U tests were employed. Though due to the small sample size of this pilot study (n = 9 HV and n = 10 FI respectively) the statistical analyses are acknowledged to be underpowered, therefore it is accepted that not all statistically significant results may be detected.

Statistical analyses were performed using a commercially available software package (SPSS Statistics Version 20: IBM, New York, USA and Prism Version 6: GraphPad Software Inc. La Jolla, USA). A P value of <0.05 was considered statistically significant.

7.6 Results

7.6.1 Healthy volunteer subject demographics

A total of 27 healthy volunteers were recruited for the study. All subjects tolerated the procedure without complication. Descriptives for participant age are shown below (Table). Of the female participants 14 were parous and 8 nulliparous. Recruitment was weighted towards parous females as this is representative of the patient cohort that usually present for assessment of anal sphincter function (Pretlove et al., 2006, Whitehead et al., 2009a).

Descriptives – HV participant age

	All (N= 27)	Female (n = 19)	Male (n = 8)
Mean	41	34	39
95% CI -	36.3	20.3	34.2
95% CI +	46.3	47.4	44.1
SD	10	16	13
Median	**41**	**29**	**37**
IQR	**17.0**	**14.0**	**22.5**
Min	22	21	21
Max	64	67	67
Skew	0.51	0.39	1.52

Table 7-I Table of healthy volunteer participant demographics subdivided by sex

7.6.2 FI patient demographics

The FI group consisted of 10 patients with a primary presenting complaint of FI. The median age was 62 (range 28-77). Nine were parous and 1 nulliparous.

Comparison of age between the groups with a Mann Whitney U test demonstrated that the FI group was significantly older than the HV group ($U = 26.5$, $z = -3.14$, $p = .002$) (Figure 7-IV).

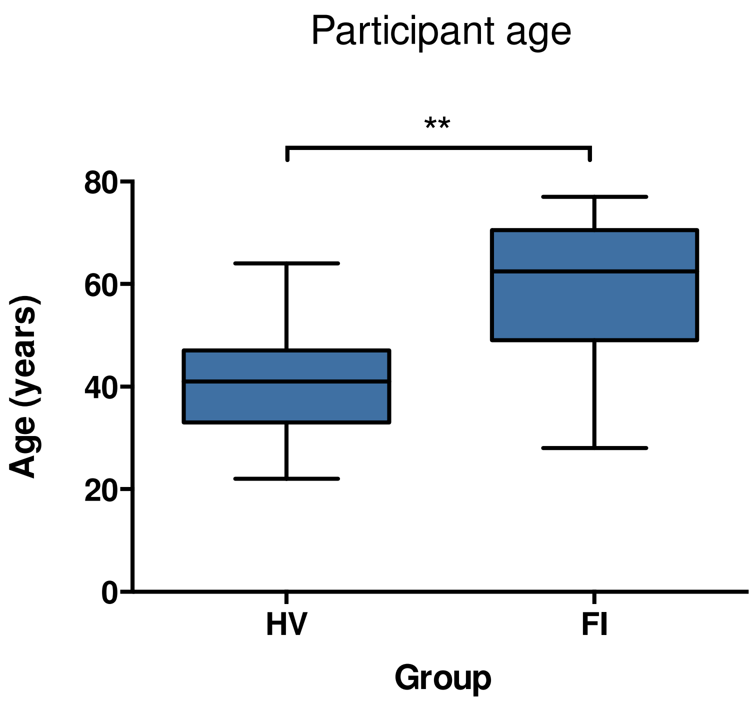

Figure 7-IV Box and whiskers plot demonstrating difference in participant age in between the female healthy volunteers (HV) (n = 19) and female patients with faecal incontinece (FI) (n = 10) groups. Whiskers represent minimum and maximum values.

7.6.3 Symptoms of disordered continence / defaecation

In the HV group there were no symptoms of bowel dysfunction.

In the FI group, 9 patients reported symptoms of faecal urgency and 8 reported symptoms of passive faecal leakage. The median duration of symptoms was 2 years (range 1 – 15 years). Five patients reported significant co-existent symptoms of constipation (Cleveland Clinic Constipation score >8). Symptom severity score descriptives for both the HV and FI groups are shown below (Table 7-II).

Group statistics - symptom severity scores

	HV (n=19)		FI (n=10)		*p* value[a]
	Median	range	Median	range	
Modified St Mark's Incontinence score (max=24)	1	0-5	15	8-20	***
Cleaveland Clinic Constipation score (max=30)	1	0-3	5	0-13	**
PAC-SYM score (max=48)	2	0-5	7	0-30	**

a. Mann Whitney U test comparing HV *vs.* FI
** *p* value < .001
*** *p* value < .0001

Table 7-II Summary table of faecal incontinence and constipation symptom scores for female healthy volunteers (n = 19) and female patients with faecal incontinence (n = 10).

7.6.4 Anal sensitivity to electrical stimulation

All HV participants demonstrated anal sensory thresholds to electrical stimulation at 1cm within the normal range.

Median anal sensitivity to electrical stimulation for the HV group as a whole was 4.7mA (IQR 2), females 4.6 mA (1.6) and males 5.0 (3.2). Visual inspection of distribution plots and normality testing indicated a normal distribution (Table 7-III). An independent samples T test demonstrated no difference in anal sensitivity between males and females (p = 0.380).

Descriptives – HV anal sensitivity to electrical stimulation

	All (N= 27)	Female (n = 19)	Male (n = 8)	*p* value[a]
Mean	4.69	4.47	5.21	
95% CI -	4.13	3.88	3.74	
95% CI +	5.25	5.07	6.69	
SD	1.42	1.24	1.77	
Median	**4.70**	**4.60**	**4.95**	0.380 (n.s.)
IQR	**2.00**	**1.60**	**3.18**	
Min	1.90	1.90	2.90	
Max	8.00	6.80	8.00	
Skewness	0.37	-0.20	0.52	

a. Mann Whitney U test comparing males *vs*. females

Table 7-III Table of descriptives for anal sensitivity to electrical stimulation at 1cm (1Hz frequency, 1ms pulse width) for all healthy volunteer participants and subdivided by sex.

With regards to the patient group, six out of 10 patients with FI demonstrated hyposensitivity to anal stimulation (i.e. increased thresholds to stimulation).

A Mann Whitney U test demonstrated that anal sensory thresholds were significant higher in the incontinent group (HV median 4.6 mA *vs.* FI median 11.1 mA, U = 8.0, z = -3.99, p = 0.001) (Figure 7-V).

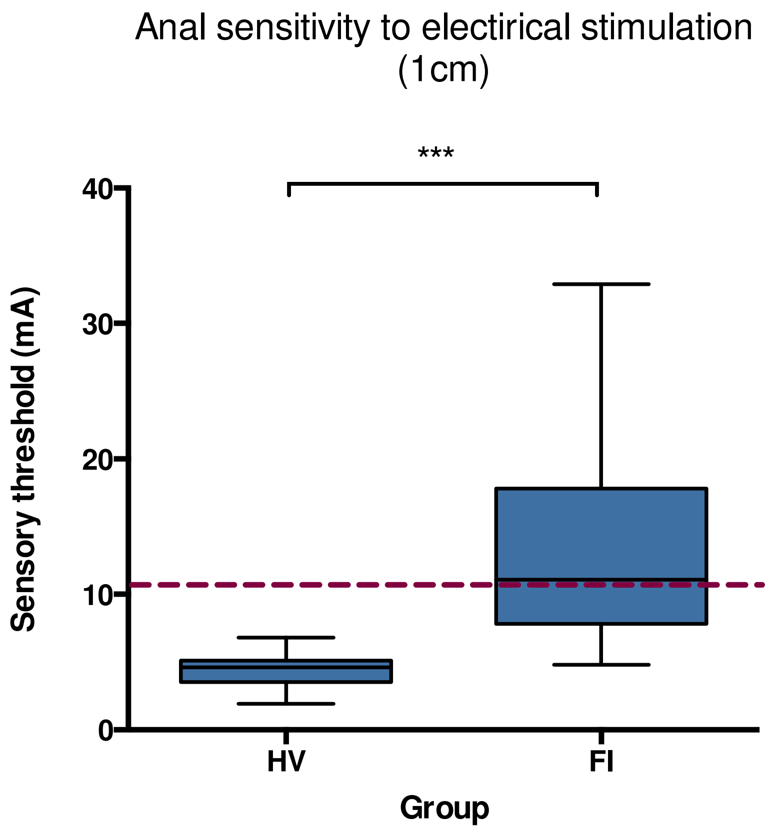

Figure 7-V Box and whiskers plot demonstrating difference in anal sensitivity to electrical stimulation at 1cm (1Hz frequency, 0.1 ms pulse width) between female healthy volunteers and female patients with faecal incontinence. The maroon dotted line represents the upper limit of normal (10.4 mA). Whiskers represent minimum and maximum values.

7.6.5 Rectal sensitivity to balloon distension

All healthy volunteer participants demonstrated normal rectal sensitivity to balloon distension. Data are displayed in Table 7-IV below. Visual inspection of distribution plots and normality testing demonstrated that the data were normally distributed. Mann Whitney U test demonstrated no sex difference in FCS (p = .549), DDV (p = .549) and MTV (p = 481).

Descriptives - Rectal sensory thresholds to balloon distension

	All (N = 27)			Female (n = 19)			Male (n =8)		
	FCS	DDV	MTV	FCS	DDV	MTV	FCS	DDV	MTV
Mean	41	111	186	41	109	181	41	116	197
95% CI -	33.0	95.7	164.4	32.6	89.4	153.9	18.0	86.6	155.2
95% CI +	49.2	125.6	206.9	49.9	127.8	207.5	63.3	144.4	239.5
Std. Deviation	20.5	37.8	53.7	18.0	39.8	55.6	27.1	34.6	50.4
Median	**35**	**109**	**180**	**36**	**100**	**180**	**32**	**113**	**186**
Interquartile Range	**27**	**38**	**80**	**23**	**38**	**95**	**32**	**49**	**75**
Minimum	19	55	109	19	55	109	21	60	149
Maximum	100	180	290	83	180	290	100	170	290
Skewness	1.3	0.5	0.5	0.9	0.7	0.6	1.9	0.2	0.8

Table 7-IV Table of rectal sensory thresholds to balloon distension in all females, nulliparous females, parous females and males. Data are displayed as median (IQR). FCS = first constant sensation, DDV = defaecatory desire volume, MTV = maximum tolerated volume. Normal values have been previously described (Mohammed et al., 2010a)

In the FI group, none were found to have rectal hypersensitivity (2/3 reduced thresholds to rectal balloon distension). Two patients in the FI group were found to have rectal hyposensitivity (2/3 elevated thresholds to rectal balloon distension).

Mann Whitney U demonstrated no overall group difference in FCS (p = .148), DDV (p = .142) or MTV (p = .765) between the healthy females and females with faecal incontinence. These data are summarized in Table 7-V below.

Group statistics - rectal sensitivity to balloon distension

	HV (n=19)		FI (n=10)		p value[a]
	Median	range	Median	range	
First constant sensation (mls)	36	19-83	48	23-160	n.s.
Defaecatory desire volume (mls)	100	55-180	114	86-245	n.s.
Maximum tolerated volume (mls)	180	109-290	174	108-340	n.s.

a. Mann Whitney U test comparing HV *vs.* FI
n.s. not significant

Table 7-V Table demonstrating rectal sensory thresholds to balloon distension in female healthy volunteers (HV) (n = 19) and female patients with faecal incontinence (FI) (n = 10). Data are displayed as median and range.

7.6.5 Anal sphincter function

When described using the traditional measures described in Chapter 4, all healthy volunteers both male and female had normal anal sphincter function at rest and during squeeze.

HRAM-SP-5 and HRAM-SP-30 were also calculated (although no normal values for these instruments exist for males). Using the novel HRAM-SP-5, one female (parous) had a profile squeeze below the 5th percentile (used as the lower limit of normality) as described in chapter 5. This participant remained in the analysis.

In the FI group, using the traditional measures described in Chapter 4, one (1/10 [10%]) patient had a reduced functional anal canal length, 2 (2/10 [20%]) patients had a reduced average anal resting pressure and 7 (7/10 [70%]) had a reduced average incremental anal squeeze pressure. Using the novel measures, 2 (2/10 [20%]) had a reduced HRAM-RP and 7 (7/10 [70%]) had a reduced HRAM-SP-5. These data are summarized in Table 7-VI below.

Mann Whitney U demonstrated significant differences in the maximum incremental anal squeeze pressure (U = 30.5, z = -2.96, *p* = 0.003) and HRAM-SP-5 (U = 29.0, z = -3.03, *p* = 0.002) between healthy females and females with FI.

Manometric measures of anal sphincter function		HV Males (n = 8)	HV Females (n=19)	FI Females (n=10)	p value[a]
Rest	Functional anal canal length (cm)	3.8 (2.4 - 6.2)	3.4 (2.4 - 5.6)	3.7 (1.5 - 5.4)	n.s.
	HRAM-RA (mmHg)	68 (38 - 137)	70 (42 - 111)	58 (18 - 90)	n.s.
	HRAM-RP (mmHg.cm.30sec)	199 (89 - 360)	167 (79 - 296)	124 (27 - 277)	n.s.
Squeeze	HRAM-SI (mmHg)	213 (126 - 358)	108 (35 - 287)	21 (3 - 318)	**
	HRAM-SP-5 (mmHg.cm.5sec)	490 (250 - 1188)	481 (170 - 987)	169 (45 - 1022)	**

a. Mann Whitney U test comparing female HV and FI
n.s. not significant
** *p* value < .001

Table 7-VI Table of manometric measures of anal sphincter function in healthy volunteers (female [n = 19] and male [n = 8]) and female patients with faecal incontinence (n=10). Data are displayed as median (minimum – maximum). Mann Whitney U test compare female HV and patients with FI

7.6.6 Transient anal sphincter relaxation characteristics in health – subjective description

Relaxations of the anal sphincter in health were clearly identified using the high-resolution system. Figure 7-VI demonstrates a 100 second screenshot of anorectal pressures in a single subject displayed using a colour contour plot.

This plot clearly displays the anal sphincter as a band of green seen centrally. Inferior to this the colour is orange, indicating higher pressures due to weight on the distal sensor (as the patient is in the sitting position). The area superior to the anal canal is blue, representing lower pressures within the rectum.

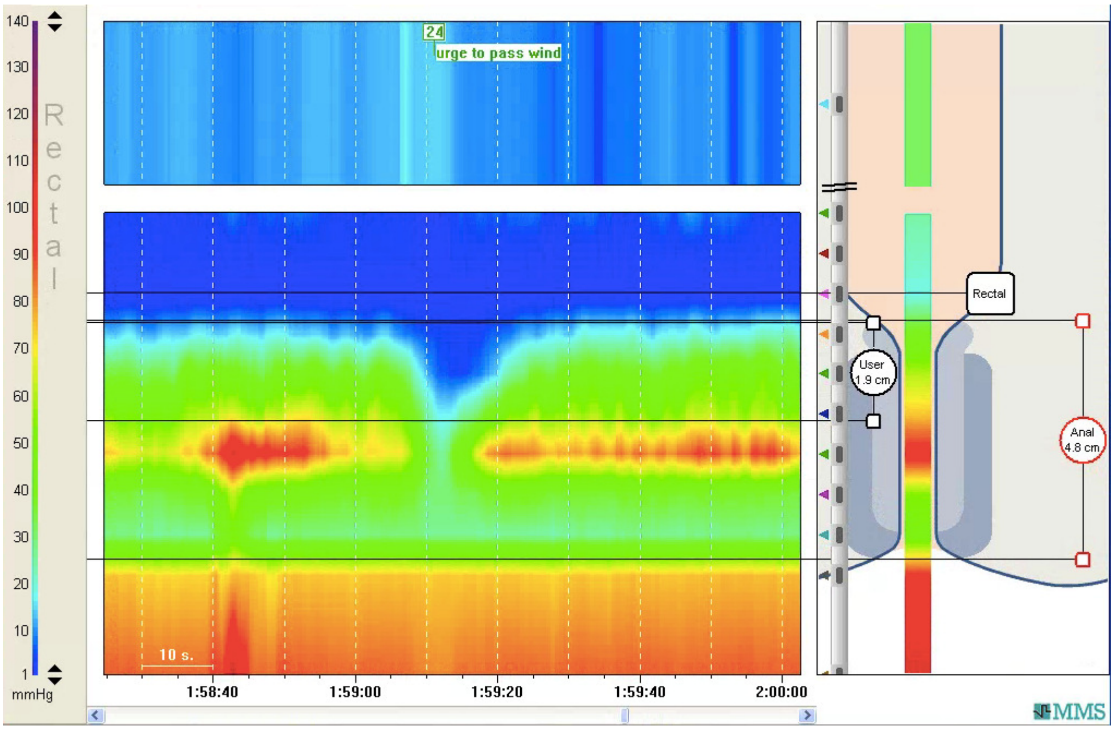

Figure 7-VI Colour contour plot from a single participant demonstrating a transient anal sphincter relaxation. In this diagram cool (blue) colours represent low pressures and warmer (red) colours represent high pressures. The anal canal is represented as a band of green. In the centre of the picture, the pressures within the upper anal canal are seen to fall (represented as a change in colour from green to blue). At the same time pressures more proximally (in the box above) are seen to rise slightly and the participant has reported the urge to pass wind.

After a period of about 30 seconds a relaxation of the anal sphincter is seen. There is a colour change in the upper anal canal with the previously green pressures appearing blue. This illustrates a relaxation, most predominantly of the upper portion of the anal sphincter. The colour change resolves spontaneously after approximately 20 seconds.

Simultaneously, a slight change is seen in the upper box (which illustrates pressure in the most proximal 'balloon' sensor). This change in colour from blue to light blue indicates a slight increase in pressure. A note from the investigator marks that the participant has reported the concurrent urge to pass wind.

When viewed as a manometric line plot (Figure VII) the same sphincter relaxation is seen as a drop in pressures in the upper 4 sensors of the anal canal. The modest increase in rectal pressure is much more difficult to see.

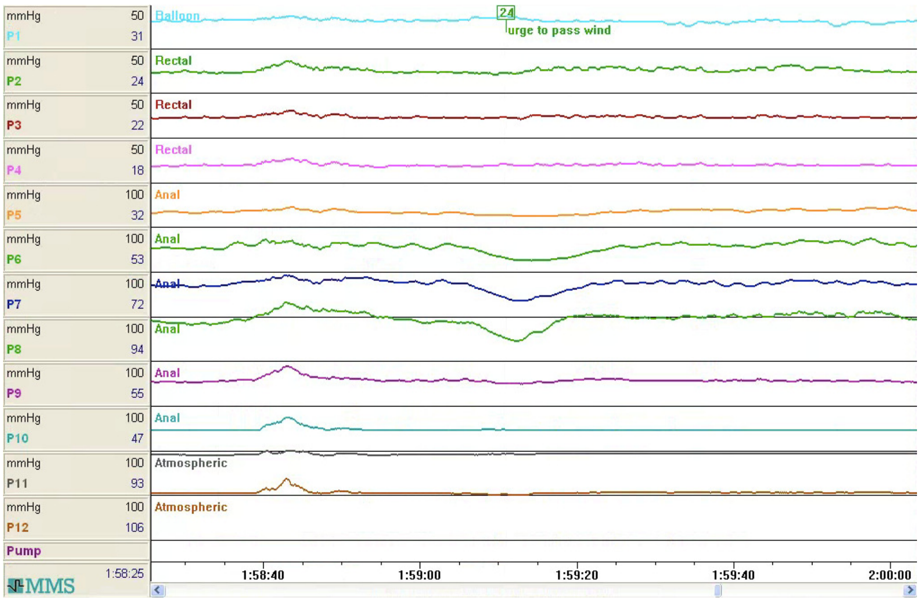

Figure 7-VII Manometric line tracing of the period demonstrated in Figure 7-VI. The more superior traces represent sensors more proximally (i.e. within the rectum) and the inferior traces represent the sensors more distally (i.e. in the distal anal canal and reference outside the body). A TASR is seen in the central portion of the plot, indicated by a fall in recorded pressures within the upper anal canal.

In addition, close inspection of line traces revealed that relaxations of the anal canal were not only associated with reduction in absolute pressures, but were also characterized by loss of supra-imposed pressure oscillations (typically seen as cyclical variations in pressure occurring at a rate of approximately 30/minute). This was observed as 'smoothing' of individual traces was postulated to be indicative of sphincteric inhibition.

In some individuals, prominent cyclical slow waves are seen. These were distinguishable from sphincter relaxations due to their rhythmic nature and persistence of the aforementioned superimposed pressure oscillations indicating a lack of inhibition of basal activity (Figure 7-VIII).

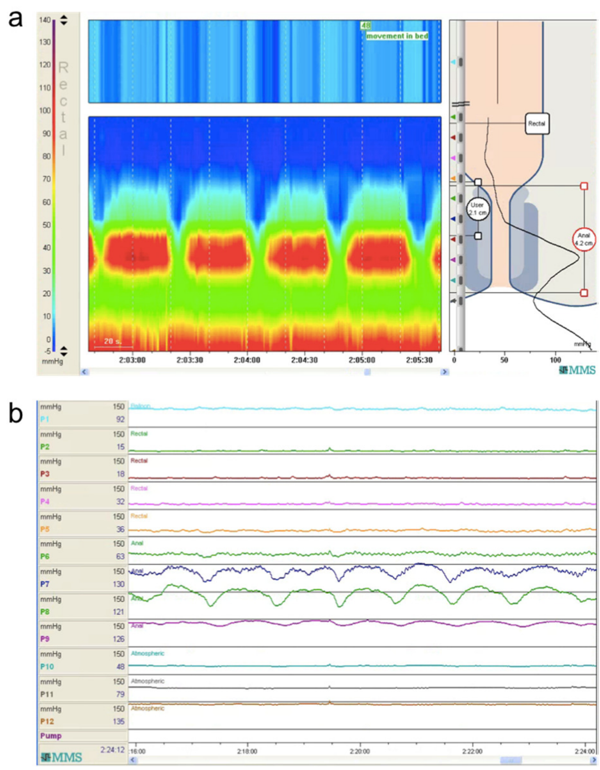

Figure 7-VIII Combined (a) colour contour plot and (b) colour contour plot of 180 seconds of rest in a single participant. Initial inspection of the colour contour plot could suggest recurrent relaxations of the anal canal, however the metrical nature of the events, together with the absence of loss of basal activity in the line trace suggests that these are in fact slow waves.

Occasionally, upper anal canal relaxations occurred in close succession, if 2 apparent relaxation events occurred within 15 seconds, they were considered as a single TASR (Figure 7-IX).

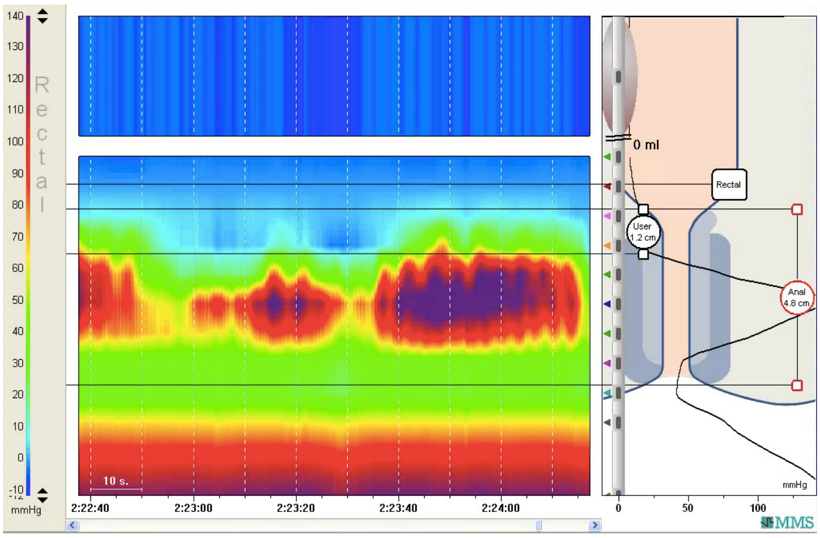

Figure 7-IX Colour contour plot from a single participant demonstrating an upper anal canal relaxation. After around 15 seconds there appears to be a temporary of the relaxation however a further relaxation is seen immediately following. This event was considered as a single TASR.

7.6.7 Prolonged sphincter function at rest in faecal incontinence – subjective description

Quality and appearance of sphincter pressures in the FI group were more variable.

Particularly in those with reduced resting anal tone, appreciation of variations in sphincter tone was more difficult to recognize using the colour contour plots. In this recording in the left lateral position, pressures within the anal are globally low (the anal canal is depicted as light blue inferior to the darker blue colour denoting slightly lower pressures within the rectum) with the margins of the anal sphincter more difficult to recognize (Figure 7-X).

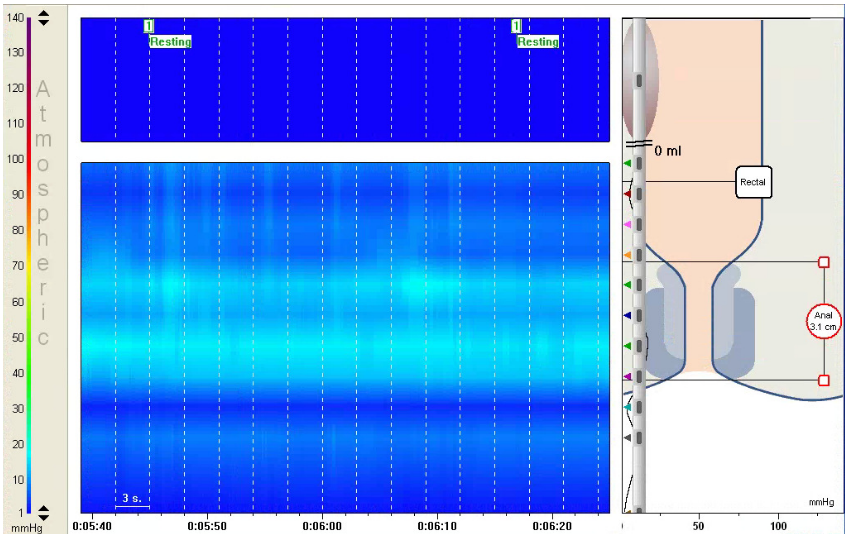

Figure 7-X Colour contour plot from a single patient with FI demonstrating globally low anal sphincter pressures at rest in the left lateral position. The anal canal is represented as a band of light blue signifying marginally higher pressure than the darker blue of the rectum, which appears more superiorly.

When the patient is moved to the sitting position, the anal canal (seen as a band of green in the central portion of the picture) is easier to recognize however the boundary of the distal canal is somewhat indistinct (Figure 7-XI).

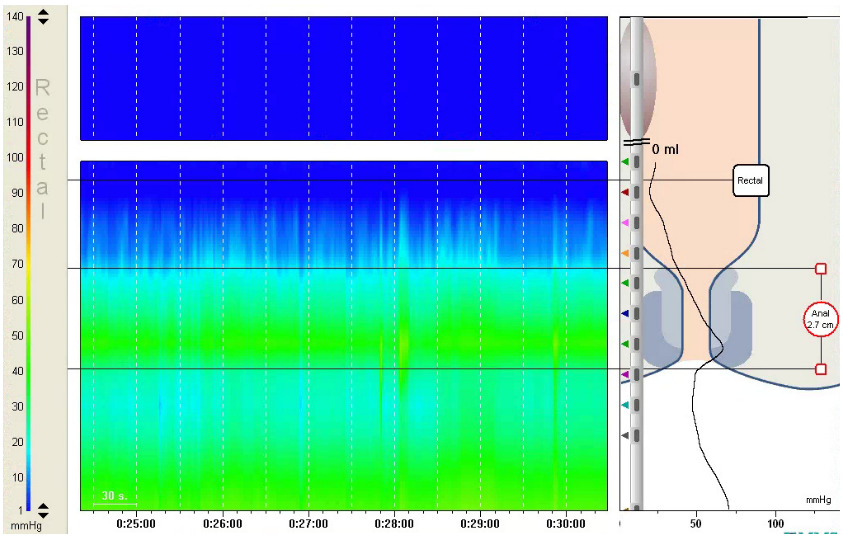

Figure 7-XI Colour contour plot of the same individual as in Figure 7-X, now in the sitting position. The difference between the anal and rectal pressures is now more marked with the anal canal seen as a band of green centrally in the picture.

In incontinent patients, general anal tone appeared to change following meal consumption. Four individuals (4/10 [40%]) demonstrated a general alteration of anal activity in the postprandial period. This was characterised by more disordered manometric morphology of the anal canal (Figure 7-XII).

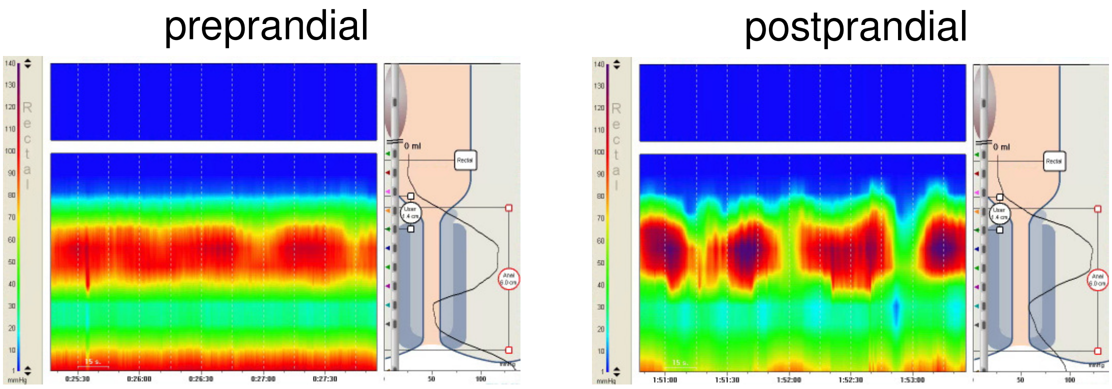

Figure 7-XII Two minute colour contour plots from a single individual with faecal incontinence pre- and post prandially. Anal sphincter pressures have a more unstable / disordered appearance in the postprandial period.

In 2 individuals with FI, the postprandial period was characterised by long periods of significantly reduced anal tone (lasting up to 30 minutes). These events were not perceived by the respective patients (Figure 7-XIII).

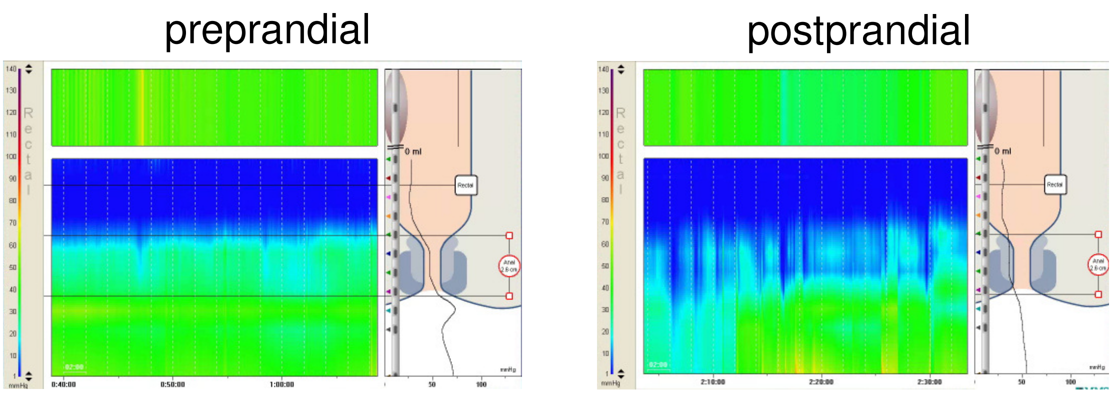

Figure 7-XIII Thirty minute colour contour plots from a single individual with faecal incontinence pre- and post prandially. Anal sphincter pressures throughout the anal canal are globally low for a 30 minute period the postprandially.

However, in the FI group, individual TASRs, as described in HVs in Chapter 7.6.6 were rarely seen.

7.6.8 Baseline TASR frequency

In the full sample of HV, TASRs were uncommon events at baseline. Median TASR count was 1 (IQR 2) during the 45-minute recording period however in 2 individuals TASRs occurred with greater frequency (7 in a male participant and 11 in a nulliparous female participant). TASRs were not present at baseline in 13/27 participants.

In the female HV at baseline, median TASR count was 0 (IQR 2) during the 45-minute recording period however in 2 individuals TASRs occurred with greater frequency (4 and 11 counts in two respective nulliparous participants). TASRs were not present at baseline in 10 (10/19 [53%]) female HVs.

In the FI group TASRs were not present at baseline in 8 (8/10 [80%]) participants. The median TASR count was 0 (IQR 0.25). The greatest number of baseline TASRs recorded in a single individual with FI was 2.

Mann Whitney U demonstrated that there was no significant difference in TASR count at baseline between the two groups (U = 66.5, z = -1.5, p = .133).

7.6.9 Effect of meal consumption on TASR frequency in health

Of the 27 participants, meal consumption was associated with an increase in TASR count in 18 participants compared to pre-prandial period. No difference was observed in TASR count in 7 participants and a reduction in TASR count was observed in 2 participants. Five participants (all female) exhibited no TASRs in either the pre- or the post-prandial period. This is illustrated in Figure 7-XIV.

Shapiro-Wilk testing indicated a non normal distribution pre- and post-prandially ($p < .0001$). A Wilcoxon signed-rank test determined that there was a highly significant increase in median TASR count following meal consumption compared to baseline (3 (IQR 1-8) vs. 1 (0-2) respectively, $z = 3.72$, $p = .001$).

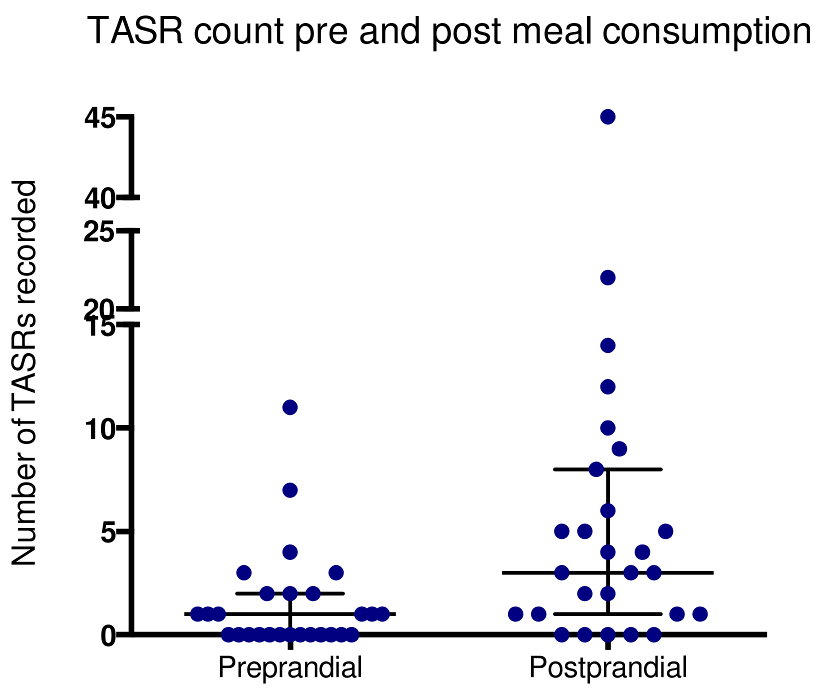

Figure 7-XIV Column dot plot demonstrating TASR count for the whole HV group (N=27) during the 45-minute preprandial and postprandial periods

Inspection of frequency dot plots revealed one obvious outlier (a 31-year-old female) who exhibited 47 TASRs in the postprandial period relative to a median of 3 in the full sample. After applying a filter to exclude this case, the pre- / post-prandial count difference remained significant ($p = .001$) therefore a decision was made to retain the outlier.

To explore if there were sex differences in TASR count before and after meal consumption, a 2x2 mixed ANOVA with time as the within subject variable (pre- and post- prandially) and sex as the between subjects variable (male and female) was performed. This revealed that there was no interaction effect of meal consumption by sex (F (1,24) = .062, p = .806, ηp^2 = .003 with an observed power 57%) (Figure 7-XV).

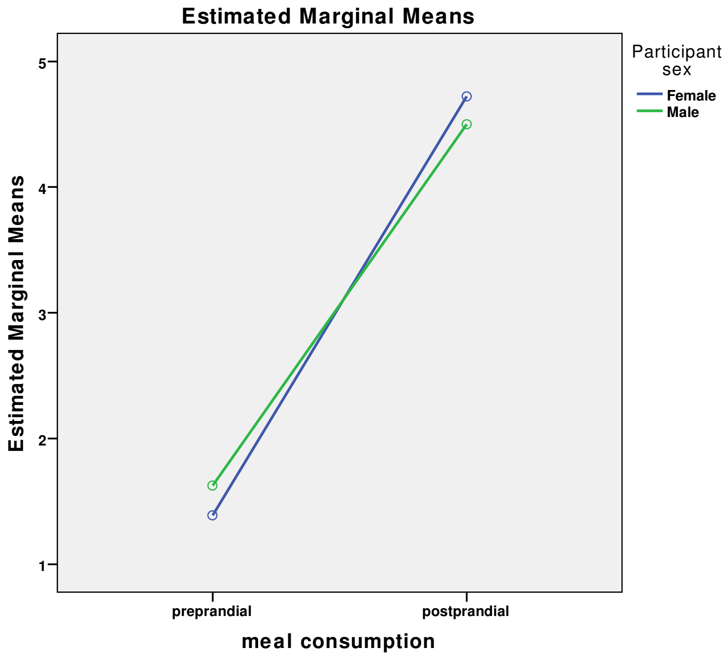

Figure 7-XV Line graph of estimated marginal means of TASR count pre- and post- prandially according to participant sex. This clearly shows greater marginal means for both males and females in the post-prandial period, and also that these differences are similar between sexes.

7.6.10 Effect of meal consumption on TASR frequency in faecal incontinence

Of the 10 participants in the FI group, meal consumption was associated with an increase in TASR count in 5 participants (5/10 [50%]) compared to pre-prandial period, associated with no difference in TASR count in 3 participants (3/10 [30%]) and associated with a reduction in TASR count in 2 participants (2\10 [20%]). Three participants (3/10 [30%]) exhibited no TASRs in either the pre- or the post-prandial period. A Wilcoxon signed-rank test determined that there was no difference in median TASR count following meal consumption compared to baseline (0 (IQR 0.25) vs. 0.5 (2.25) respectively, z =-1.28, p = .201). The greatest number of postprandial TASRs recorded in a single individual with FI was 5.

Of the 19 female HVs, meal consumption was associated with an increase in TASR count in 9 participants (9/19 [47%]) compared to pre-prandial period, associated with no difference in TASR count in 7 (7/19 [37%]) participants and associated with a reduction in TASR count in 1 participant (1/19 [5%]). Five participants (5/19 [26%]) exhibited no TASRs in either the pre- or the post-prandial period. A Wilcoxon signed-rank test determined that there was a significant increase in median TASR count following meal consumption compared to baseline (0 (IQR 2) vs. 3 (9) respectively, z = -2.97, p = .003) in the HV group.

Mann Whitney U demonstrated that difference in TASR count between the two groups postprandially was approaching significance, however not statistically significant (U = 54.5, z = -1.93, p = .057). A paired line plot (Figure 7-XVI) demonstrates the TASR count pre and post meal consumption in both groups below.

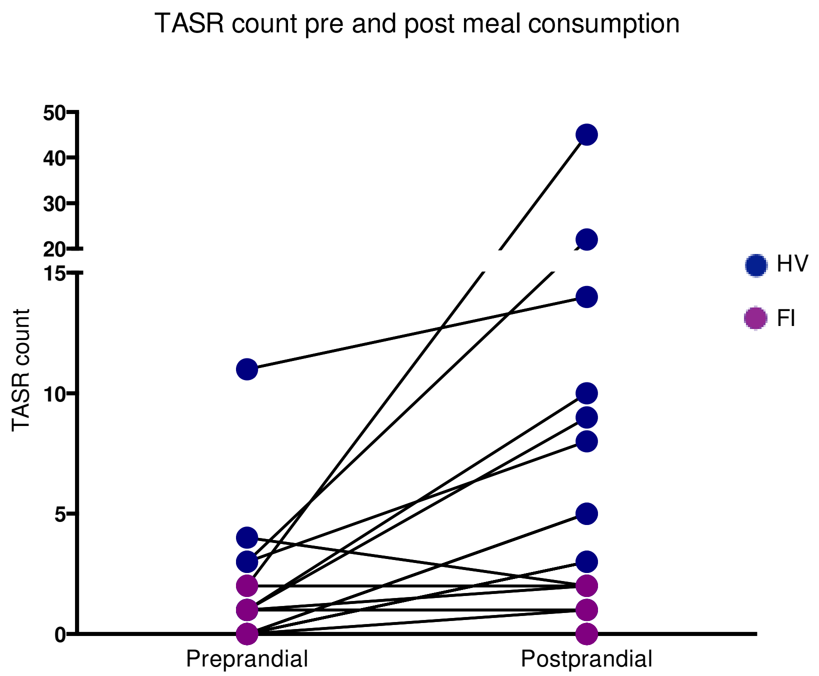

Figure 7-XVI paired line plot of TASR count pre and post prandially in HVs (blue dots) and patients with FI (purple dots) demonstrating individual differences in TASR counts pre and postprandially.

Further exploration of group differences (female HV *vs.* FI) in TASR count pre and post prandially was attempted using a 2x2 ANOVA however was not possible due to the small group sample sizes (mixed 2x2 ANOVA reported an observed power of 27%, when controlling for age using a 2X2 ANCOVA observed power was 8%). Nevertheless, inspection of estimate marginal means plots pointed towards a possible interaction effect between participant group and meal consumption (Figure 7-XVII).

A further power calculation demonstrated that should interaction differences (group and meal consumption) be sought, a total sample size of 111 individuals (based on large effect size with 80% power) would be required to effectively reduce the rate of type II error.

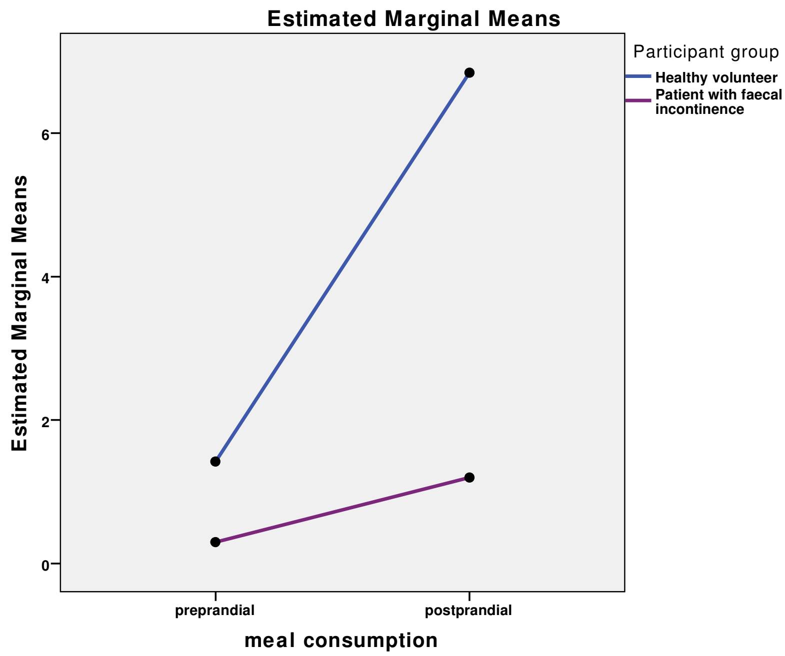

Figure 7-XVII Line graph of estimated marginal means of TASR count pre- and post- prandially according to participant group. This shows greater estimated marginal means for both female HV and FI groups in the post-prandial, when compared to the pre-prandial period. There appears to be a reduced pre – to post prandial difference in the FI group.

7.6.11 TASR characteristics – morphology in health

To examine TASR characteristics, TASRs from all HV subjects were pooled and examined. In the HV group as a whole, 207 TASRs were observed (159 in 15 female participants and 48 in 8 male participants). Visual inspection of distribution histograms and normality testing revealed that all data except TASR rectal pressure were normally distributed. Descriptives for all TASR characteristics are displayed in below in Tables 7-VII and 7-VIII.

Descriptives – HV TASR characteristics

			Mean	SD	95% CI -	95% CI +	Median	IQR	Min	Max	Skew	*p* value[a]
Morphological characteristics	Duration (secs)	All	25.9	12.0	24.3	27.6	23.0	9.0	8.0	103.0	2.3	
		Female	25.2	11.7	23.3	27.0	23.0	8.0	8.0	103.0	3.0	n.s.
		Male	28.5	12.9	24.7	32.2	27.5	18.0	10.0	62.0	0.5	
	Depth (cm)	All	2.0	0.7	1.9	2.1	1.9	0.9	0.7	3.9	0.6	
		Female[b]	2.1	0.7	2.0	2.2	2.0	1.1	0.7	3.3	0.3	***
		Male	1.7	0.7	1.5	1.9	1.5	0.8	1.0	3.9	1.6	
	% Depth (% anal canal involved)	All	58.2%	24.2%	54.9%	61.5%	53.0%	35.0%	20.0%	100.0%	0.5	
		Female[b]	63.0%	23.8%	59.2%	66.7%	58.0%	41.0%	20.0%	100.0%	0.3	***
		Male	42.3%	17.7%	37.1%	47.4%	36.0%	20.0%	21.0%	100.0%	1.7	
Pre-TASR pressures	Pre-TASR rectal pressure (mmHg)	All	22.6	7.5	21.6	23.6	22.0	12.1	9.7	49.7	0.6	
		Female	21.5	6.7	20.5	22.6	20.3	12.1	11.8	42.4	0.5	***
		Male[b]	26.2	8.8	23.7	28.8	27.1	9.7	9.7	49.7	0.3	
	Pre-TASR anal pressure (mmHg)	All	67.3	16.3	65.1	69.6	66.3	25.1	27.0	110.8	0.3	
		Female	65.0	14.5	62.8	67.3	65.0	20.0	27.0	100.0	0.1	***
		Male[b]	75.0	19.8	69.2	80.7	77.0	27.0	36.7	110.8	-0.1	

a. Independent samples T test comparing TASRs observed in HV males *vs.* HV females
b. significantly greater than comparative group
c. significantly greater change than comparative group

* *p* value < .05
*** *p* value < .0001
n.s. no statistically significant difference

Table 7-VII Table of TASR characteristics (morphological and pre-TASR pressures). Data pertains to all TASRs observed during the study period (N = 207). Means testing analysis demonstrates significant differences in some TASR characteristics between HV males and females.

Descriptives – HV TASR characteristics

			Mean	SD	95% CI -	95% CI +	Median	IQR	Min	Max	Skew	*p* value[a]
TASR pressures	TASR rectal pressure (mmHg)	All	29.2	13.7	27.3	31.1	25.6	16.4	12.2	100.0	1.6	
		Female	29.9	14.6	27.6	32.1	26.3	17.7	12.2	100.0	1.6	n.s.
		Male	27.0	10.1	24.1	29.9	24.5	14.0	13.3	56.0	0.9	
	TASR anal pressure (mmHg)	All	40.1	16.2	37.8	42.3	38.0	19.4	0.0	131.5	1.7	
		Female	36.8	12.4	34.9	38.8	36.0	15.8	0.0	75.6	0.5	***
		Male[b]	50.8	21.8	44.4	57.1	44.0	29.4	25.3	131.5	1.6	
	TASR anal min pressure (mmHg)	All	23.2	8.2	22.1	24.4	23.0	11.0	0.0	69.0	1.2	
		Female	23.2	9.0	21.8	24.6	22.0	14.0	0.0	69.0	1.2	*
		Male[b]	23.3	5.0	21.8	24.7	23.0	4.8	13.0	37.0	0.2	
TASR pressure changes	Anal pressure change (mmHg)	All	-27.3	13.8	-29.2	-25.4	-26.8	17.5	-79.8	28.8	-0.1	
		Female	-28.2	13.0	-30.2	-26.2	-27.5	18.0	-79.8	11.3	-0.3	n.s.
		Male	-24.2	16.0	-28.9	-19.6	-22.9	16.7	-70.1	28.8	0.1	
	% Anal pressure change (%)	All	-40.3%	17.2%	-42.7%	-38.0%	-41.3%	21.8%	-100.0%	28.0%	2.8	
		Female[c]	-42.7%	16.5%	-45.2%	-40.1%	-42.5%	24.1%	-100.0%	20.5%	0.4	***
		Male	-32.7%	17.5%	-37.7%	-27.6%	-34.7%	20.0%	-63.2%	28.0%	1.0	
	Rectal pressure change (mmHg)	All	6.6	12.6	4.8	8.3	2.8	8.7	-13.0	86.5	2.8	
		Female[c]	8.3	13.6	6.2	10.5	3.5	9.5	-5.3	86.5	2.6	***
		Male	0.7	5.8	-0.9	2.4	0.0	6.2	-13.0	19.5	0.4	
	% Rectal pressure change (%)	All	35%	73%	25%	45%	13%	40%	-43%	641%	4.3	
		Female[c]	44%	80%	31%	56%	17%	48%	-25%	641%	3.9	***
		Male	5%	23%	-2%	12%	0%	24%	-43%	77%	0.7	

a. Independent samples T test comparing TASRs observed in HV males *vs.* HV females
b. significantly greater than comparative group
c. significantly greater change than comparative group

* *p* value < .05
*** *p* value < .0001
n.s. no statistically significant difference

Table 7-VIII Table of TASR characteristics (TASR pressures and TASR pressure changes). Data pertains to all TASRs observed during the study period (N = 207). Means testing analysis demonstrates significant differences in some TASR characteristics between males and females.

All data in the text are expressed as mean ± standard deviation unless otherwise specified. When considering all 207 observed TASRs in health, analysis revealed that TASRs typically lasted 25 ± 12 seconds and involved 52.2% ± 24.2% of the anal canal.

TASRs in health were associated with a significant reduction in anal pressure (pre-TASR anal pressure 67.3 ± 16.3 mmHg *vs.* TASR anal pressure 40.1 ± 16.1 mmHg (95% CI 25.4 to 29.1), $t(206) = 28.4$, paired sample T test $p < .0001$) (Figure 7-XVIII). This resulted in an average TASR anal pressure change of -40.3 ± 17.2%.

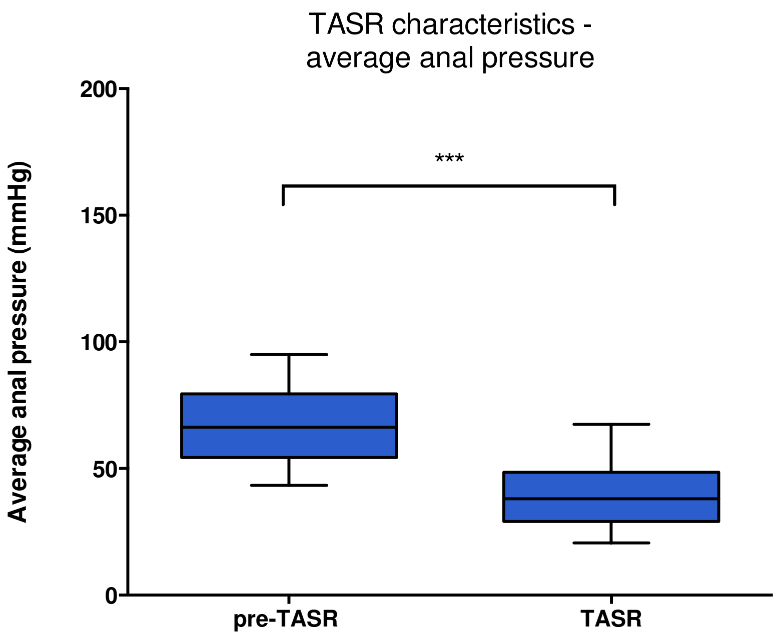

Figure 7-XVIII Box and whiskers plot demonstrating change in average anal pressure during TASRs. Whiskers represent the 5th and 95th percentile. N = (207). *** = $p < .001$.

TASRs were also generally associated with a small but significant increase in rectal pressure (pre-TASR rectal pressure 22.6 ± 7.5 mmHg *vs.* TASR rectal pressure 29.2 ± 13.7 mmHg (95% CI -8.3 to -4.8), $t(206) = -7.5$, paired sample T test $p < .0001$) (Figure 7-XIX). This resulted in an average TASR rectal percentage pressure change (increase) of 35 ± 73%.

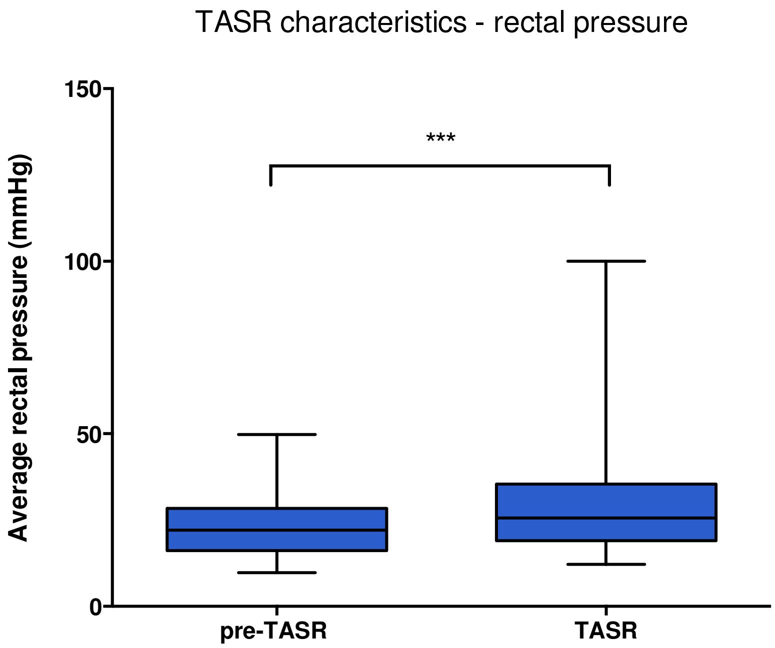

Figure 7-XIX Box and whiskers plot demonstrating change in average rectal pressure during TASRs. Whiskers represent the 5th and 95th percentile. N = (207). *** = $p < .001$.

7.6.12 TASR characteristics – morphological correlates

To further examine the association between TASR characteristics of interest, two-tailed Pearson correlations were performed.

In health, this demonstrated that that was no significant correlation between TASR rectal pressure and average anal pressure change $r(98) = 0.05$, $p = .410$ nor was there any correlation between % TASR rectal pressure change and % TASR anal pressure change $r(98) = 0.09$, $p = .249$.

There was however a small positive correlation between TASR depth and duration $r(98) = -0.162$, $p = .02$ with longer lasting TASRs involving a greater length of the anal canal.

7.6.13 TASR characteristics – associations with male or female sex in health

Whilst accepting that this study is not powered to examine differences in TASR characteristics between male and female participants, some exploratory analyses were performed to explore differences in characteristics of TASRs between sexes.

As expected, some baseline variables differed between males and females.

Pre-TASR anal and pressures were significantly higher in males than females (male mean pre-TASR anal pressure 74.9 ± 19.8 mmHg *vs.* female 65.0 ± 14.5 mmHg [95% CI, -15.1 to -4.8], $t[205] = -3.8$, Independent sample T test $p < .0001$) as were pre-TASR rectal pressures [male mean pre-TASR rectal pressure 26.2 ± 8.8 mmHg *vs.* female 21.5 ± 6.7 mmHg [95% CI, -7.1 to -2.3], $t[205] = -3.9$, Independent sample T test $p < .0001$).

Interestingly there were some differences in TASR morphology between males and females.

TASRs observed in females typically involved a greater absolute length of the anal canal (male mean TASR depth 1.7 ± 0.7 cm *vs.* female 2.1 ± 0.7 cm [95% CI, 1.9 to 0.7], $t[205] = 3.5$, Independent sample T test $p < .0001$) and involved a greater percentage length of the anal canal (male mean % TASR depth 42% ± 17% *vs.* female 62% ± 23% [95% CI, 13 to 28], $t[205] = 3.5$, Independent sample T test $p < .0001$).

Despite no difference in the average anal pressure change (male mean anal pressure change -24.2 ± 16.0 mmHg *vs.* female -28.2 ± 13 mmHg [95% CI, -8.4 to 0.5], $t[205] = -1.8$, Independent sample T test $p = .081$) there was a significant difference in % anal pressure change during the TASR events between males and females (male mean % anal pressure change -32% ± 18% *vs.* female 43% ± 17% [95% CI, -15 to -4.5], $t[205] = 3.8$, Independent sample T test $p < .0001$) with

TASRs in females resulting in a greater percentage reduction in anal pressure than males.

7.6.14 TASR characteristics – morphological comparisons in health and faecal incontinence

In female subjects studied, 170 TASRs were identified: 159 in the HV group and 10 in the FI group. Whilst accepting that this study is not powered to examine differences in TASR characteristics between participant groups, some exploratory analyses were performed to explore differences in characteristics of TASRs in HV and FI with data displayed in Table 7-IX below.

When cautiously interpreted, Mann Whitney U tests demonstrated that TASRs seen in patients with FI involved a smaller percentage anal canal length (58% in HV *vs.* 49% in FI, p = .001) and were associated with a less profound decrease in anal pressure (median TASR anal pressure 36mmHg in HV *vs*. 49mmHg in FI, p = .017; median % anal pressure change -43% in HV *vs.* -24% in FI, p = .002).

Comparison statistics – female HV and FI TASR characteristics

		HV (n=157) median	HV IQR	FI (n=10) median	FI IQR	p value[a]
Morphological characteristics	Duration (secs)	23	8	29	38	n.s.
	Depth (cm)	2	1.1	1.7	1.1	n.s.
	% depth (% anal canal involved)	58%	41%	49%	62%	***
Pre-TASR pressures	Pre-TASR rectal pressure (mmHg)	20	12	31	4	***
	Pre-TASR anal pressure (mmHg)	65	20	72	27	n.s.
TASR pressures	TASR rectal pressure (mmHg)	27	18	36	7	*
	TASR anal pressure (mmHg)	36	15	49	27	*
	TASR anal min pressure (mmHg)	22.6	14	39	10	*
TASR pressure changes	Anal pressure change (mmHg)	-27.5	18	-19	13	*
	% Anal pressure change (%)	-43	24	-24	13	*
	Rectal pressure change (mmHg)	3	10	3	7	n.s.
	% Rectal pressure change (%)	17	48	9	24	n.s.

a. Mann Whitney U test comparing HV *vs.* FI
n.s. not significant
* p value < .05
*** p value < .0001

Table 7-IX Table 7-X Summary table of TASR characteristics in female healthy volunteers (HV) (total number of TASRs in HVs = 157) and female patients with faecal incontinence (FI) (total number of TASRs in patients with FI = 11).

7.6.15 TASR characteristics – perception in health

Of the 207 TASRs recorded, frequency analyses demonstrated that 97 (47%) of TASRS were perceived (Table 7-XII).

Frequency – HV TASR perception type

		Frequency	Percent
Not perceived		110	53.1
Perceived	Urge to pass wind	66	31.9
	Urge to pass stool	29	14
	Abdominal cramp/pain	1	0.5
	Other	1	0.5
Total		207	100

Table 7-XII Frequency table of TASR perception type.

Comparison of means demonstrated that perceived TASRs involved a greater length of the anal canal and greater % length of the anal canal than TASRs that were not perceived: perceived events TASR depth 2.1 ± 0.8 cm *vs.* non perceived 1.9 ± 0.6 cm (95% CI, -0.45 to 0.04), $t(205) = -2.4$, Independent sample T test p = .002 and perceived events % TASR depth 62% ± 26% *vs.* non perceived events 55% ± 21% (95% CI, -14.1% to -4%), $t(205) = -2.3$, Independent sample T test p = .02.

However there was no difference in TASR duration, average TASR anal pressure change or average TASR rectal pressure change between perceived and non-perceived events. These data are displayed in Table 7-XIII below.

Group statistics – HV TASR characteristics

			Mean	SD	*p* value[a]
Morphological characteristics	Duration (secs)	Perceived	26.2	11.8	
		Not perceived	25.6	12.4	n.s.
	Depth (cm)	Perceived	1.9	0.6	
		Not perceived	2.1	0.8	**
	% Depth (% anal canal involved)	Perceived	0.5	0.2	
		Not perceived	0.6	0.3	**
Pre-TASR pressures	Pre-TASR rectal pressure (mmHg)	Perceived	23.6	7.5	
		Not perceived	21.5	7.4	n.s.
	Pre-TASR anal pressure (mmHg)	Perceived	67.3	17.0	
		Not perceived	67.4	15.7	n.s.
TASR pressures	TASR rectal pressure (mmHg)	Perceived	30.2	14.7	
		Not perceived	28.1	12.5	n.s.
	TASR anal pressure (mmHg)	Perceived	39.5	10.7	
		Not perceived	40.7	20.7	n.s.
	TASR anal min pressure (mmHg)	Perceived	24.2	6.7	
		Not perceived	22.2	9.6	n.s.
TASR pressure changes	Anal pressure change (mmHg)	Perceived	-27.8	12.1	
		Not perceived	-26.7	15.5	n.s.
	% Anal pressure change (%)	Perceived	-40.3	11.4	
		Not perceived	-40.3	22.1	n.s.
	Rectal pressure change (mmHg)	Perceived	6.6	13.8	
		Not perceived	6.6	11.2	n.s.
	% Rectal pressure change (%)	Perceived	33.7	81.6	
		Not perceived	35.6	61.2	n.s.

a. Independent samples T test comparing perceived *vs*. non perceived TASRs

***p* value < .001
n.s. no statistically significant difference

Table 7-XIII Summary table of perceived (n = 110) and non perceived (n = 97) TASR characteristics.

A further two-tailed Spearman correlation (two-tailed) found that there was a significant, though weak association between TASR perception and the TASR depth ($r(98) = 0.166$, $p = .02$) and % TASR depth ($r(98) = 0.157$, $p = .02$)

To explore if there was an association between TASR perception and sex, a 2x2 Chi-square using Fisher's exact test was performed. This demonstrated that TASR perception did not differ between males and females. (Pearson Chi-Square = 0.28, $p = .871$) (Table 7-XIV).

Crosstabulation – HV TASR perception by sex

			Sex		Total
			female	male	
TASR perception	Not perceived	Count	85	25	110
		% within Sex	53.5%	52.1%	53.1%
	Perceived	Count	74	23	97
		% within Sex	46.5%	47.9%	46.9%
Total		Count	159	48	207
		% within Sex	100%	100%	100%

Table 7-XIV Cross tabulation of TASR perception by sex

In those TASRs that were perceived, the mean VAS intensity score was 5 (2.4) (Table 7-XV).

Descriptives – HV perceived TASR intensity score

	Statistic
Mean	4.9742
95% CI -	4.4997
95% CI +	5.4487
Std. Deviation	2.35435
Interquartile Range	4
Minimum	1.5
Maximum	10
Skewness	0.73

Table 7-XV Table of descriptives for perceived TASR intensity score based on a 10 cm VAS scale for perceived TASRs only (n = 97).

To explore the correlation between TASR perception intensity and TASR characteristics of interest, two-tailed Pearson correlations were performed (Table XVI).

Correlation statistics – HV perceived TASR intensity score			
		r	*p* value
Morphological characteristics	Duration (secs)	-0.18	n.s.
	Depth (cm)	0.596	***
	% Depth (% anal canal involved)	0.577	***
Pre-TASR pressures	Pre-TASR rectal pressure	-0.137	n.s.
	Pre-TASR anal pressure (mmHg)	-0.208	n.s.
TASR pressures	TASR rectal pressure (mmHg)	0.009	n.s.
	TASR anal pressure (mmHg)	-0.368	***
	TASR anal min pressure (mmHg)	-0.199	n.s.
TASR pressure changes	Anal pressure change (mmHg)	-0.28	***
	% Anal pressure change (%)	-0.383	***
	Rectal pressure change (mmHg)	0.101	n.s.
	% Rectal pressure change (%)	0.092	n.s.

a. Two-tailed Pearson's correlation

***p value < .001
n.s. no statistically significant difference

Table 7-XVI Table of correlation statistics for TASR perception intensity (perceived TASRs only) and TASR characteristics of interest (n = 97).

This demonstrated a strong significant positive correlation between perceived TASR intensity score and TASR depth (r[98] = 0.59, p < .0001) indicating that more intensely perceived TASRs involved a greater length of the anal canal. There was also a moderate negative correlation between the TASR average anal pressure and perceived TASR intensity score (r[98] = 0.37, p < .0001) indicating that more intensely perceived TASRs were associated with lower anal pressures during TASRs.

7.6.16 TASR characteristics – perception comparisons in health and faecal incontinence

In the group of female FI patients, of the 11 TASRs that were recorded, only 2 (2/10 [20%]) were perceived. This count was different to the 74 (74/159 [47%]) experienced in female HVs.

Although it is appreciated that the study is underpowered to detect differences between TASR characteristics between the 2 groups, association between TASR perception and health status was briefly explored with a 2x2 Chi-square using Fisher's exact test. This demonstrated that TASR perception did not differ between the HV and FI subjects. (Pearson Chi-Square = 2.68, *p* = .102) (Table 7-XVII).

Crosstabulation – TASR perception by HV / FI health status

			Group		Total
			HV	FI	
TASR perception	Not perceived	Count	85	8	93
		% within Group	53.5%	80%	55%
	Perceived	Count	74	2	76
		% within Group	46.5%	20%	45%
	Total	Count	159	10	169
		% within Group	100%	100%	100%

Table 7-XVII Cross tabulation of TASR perception by group (HV = female healthy volunteers; FI = patients with faecal incontinence).

In those TASRs perceived in the female HV group, the median VAS intensity score was 5 (IQR4). Perception types in both female HV and patients with FI are described in Table 7-XVIII below. In the FI group, both perceived TASRs were in the same individual and reported as a weak urge to pass stool (TASR perception intensity score was 1.9/10 and 2.0/10 respectively). This patient did not appear dissimilar to other patients within the FI group (70 year old parous female, anal sensory threshold at 1cm = 12.9mA (hyposensate) with normal thresholds to rectal balloon distension).

Frequency - TASR perception type

			Frequency	Percent
HV	Not perceived		85	53.5
	Perceived	urge to pass wind	54	34.0
		urge to pass stool	18	11.3
		abdomial cramp/pain	1	0.6
		other	1	0.6
		Total	159	100
FI	Not perceived		8	80
	Perceived	urge to pass stool	2	20
		Total	10	100

Table 7-XVIII Frequency table of TASR type for the female HV (healthy volunteers) and FI (patients with faecal incontinence) groups.

Of particular interest were 3 TASR events in the FI group that involved the entire anal canal without perception by the individual (Figure 7-XX). As all relaxations that involved the entire anal canal length in health were perceived as the urge or the passage of wind.

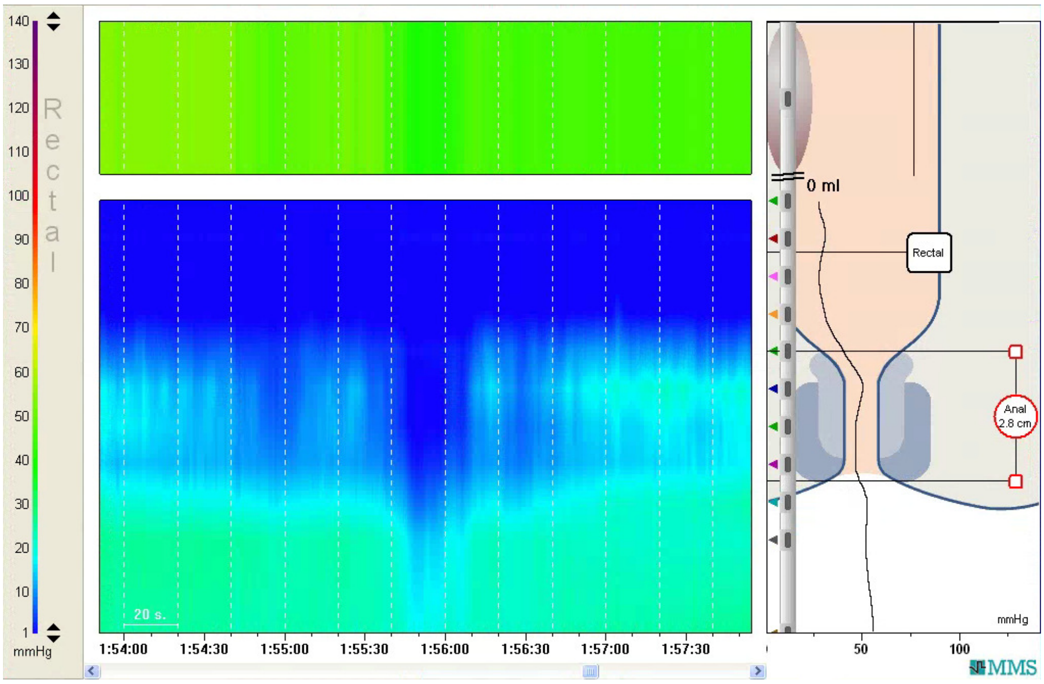

Figure 7-XX Colour contour plot in the postprandial period from a patient with faecal incontinence. A complete relaxation of the anal canal is seen. The patient does not perceive this event.

7.7 Discussion

To the author's knowledge, this is the first study that examines prolonged anorectal function in health and is the first description of transient anal sphincter relaxations using HRAM in health and faecal incontinence.

This study has demonstrated that in health, TASRs are a normal physiological finding. They occur at rest and their frequency increases following meal consumption. Relaxation of the upper anal canal appears to last on average around 25 seconds and is likely to be associated with a transient rise in rectal pressure. Approximately half of these TASRs are perceived, commonly as the urge to pass wind or the urge to pass stool. Perception and intensity of perception is associated with the length of anal canal involved. Intensity of TASR perception is also associated with the pressure change within the anal canal (the more negative the pressure change, the stronger the TASR is perceived).

These findings are in keeping with previous studies examining spontaneous anal function at rest. In a study of surgical patients without colorectal complaints in 1988, Miller et al. described spontaneous sphincter relaxations occurring more frequently than in this study (a median of 7 times per hour). Similarly however, he reported that 40% of events were perceived by the participant but did not find any association with ingestion of food (although this was only incidentally observed and informally reported) (Miller et al., 1988c). The difference in frequency noted in this study could be secondary to a number of differences in study design such as increased number of sensors within the anal canal limiting false reporting of reduction in anal pressures from movement of the catheter, differences in study fasting / feeding protocol and differences in populations studied. A second, more recent study using high-resolution colonic manometry described a similar phenomenon that the authors' termed pan colonic pressurizations. In a group of healthy volunteers, intermittent pressure increases simultaneously occurring throughout all colonic sensors associated with anal sphincter relaxations were seen. They noticed that the frequency of these events increased significantly during meals and decreased afterward with events correlated with desire to evacuate gas (Corsetti et al., 2016). This study similar in design and execution to the study described in this chapter suggests that the mechanism for TASR generation is likely to be colonic in origin.

The mechanisms which provoke TASR generation are interesting to consider. Due to the associated increase in rectal pressure during TASR onset, it seems reasonable to concur with Duthie and Bennett's proposal that TASRs are mediated in a similar fashion to the recto-anal inhibitory reflex (Cheeney et al., 2012) i.e. via inhibition of internal anal sphincter tone through activation of nitric oxide mediated mural neurons (Milligan, 1985, Wood and Kelly, 1992).

Indeed, TASR morphology as seen with HRAM appears to mirror characteristics seen during the RAIR i.e. proximal transient relaxation of the anal canal following rectal stimulation by distension (Zbar et al., 1998). The incidental finding of a flattening / loss of the basal activity on inspection of line traces from sensors within the upper anal canal during this study appears to support internal anal sphincter inhibition (although such an observation would need to be confirmed electromyographically).

Furthermore, the increase in TASR frequency following meal consumption is likely to be secondary to the known increase in rectal contractility following meal consumption (Rao et al., 2000). Whether the increase in TASR frequency is mediated independently (i.e. neurohormonally via cholecystokinin release and / or centrally via visual and olfactory stimulation) or whether it occurs secondary to the increased rectal contractility requires further investigation.

It appears reasonable to assume that the association between anal sphincter relaxations and perception is a key feature of continence. In healthy volunteers, TASR depth was associated with intensity of perception supporting the hypothesis that profound relaxations of the anal canal allow rectal contents to come into contact with the sensory apparatus of the anal canal.

When examining TASR characteristics in patients with faecal incontinence a number of differences were seen. Firstly, TASRs appeared more infrequent at baseline with little change following meal consumption secondly, TASRs appeared to involve a smaller percentage anal canal length and were associated with a smaller percentage change in anal sphincter pressure and thirdly, TASRs were rarely perceived (and in fact were only perceived by a single patient studied).

These findings are somewhat consistent with previous studies in patients with FI. The study by Miller *et al.* demonstrated a reduced frequency of anal canal relaxations in incontinent patients compared with continent controls (Miller et al., 1988a). In addition the study by Zbar *et al.* demonstrated that patients with faecal incontinence displayed an altered sphincteric response to rectal balloon distension when compared to continent controls (Zbar et al., 1998). This may explain the differences in TASR depth between HV and FI observed during this study.

It is reasonable to postulate that these alterations in TASR characteristics between health and FI could be a factor in the development of symptoms of faecal urgency. If rectal contents are intermittently 'sampled' in health, a reduction in 'sampling' frequency seen as a reduction in TASR count could result in loss of warning of the need to pass stool. This, combined with an alteration in anal sensory function could conceivably result in loss of awareness of rectal filling and the impending need to defaecate.

The influence of anal hyposensitivity on perceived anorectal events was particularly evident in the two patients with FI who displayed prolonged and profound changes in anal resting pressure postprandially. Despite the sustained comparative loss of sphincter tone, there was no perception of these events. It would be reasonable to postulate that this could be a feature of intermittent faecal leakage in this patient group.

A further interesting finding was that despite the consumption of a large meal, only one individual in the patient group described the need to defaecate during the experiment, whereas this was a common report from the healthy volunteer group. This does not seem to reflect existing anecdotal or reported evidence that meal consumption predisposes to incontinence episodes and could reflect an experimental design that was not optimized for detection of differences in the temporal response to meal consumption between the two groups.

7.7.1 Methodological limitations

The author acknowledges a number of limitations within this study. The first limitation is the short length (time) of recording. At present no ambulatory

HRAM systems exist and for this reason the participants had to remain in close proximity to the HRAM hardware and stationary in the sitting position. A 3-hour total experiment time was felt to be the longest period that could be expected without movement, which resulted in the limited 45-minute pre- and post-prandial recording periods.

The second limitation is the short length (cm) of recording within the rectum. The total recording length of the HRAM catheter is 12cm; therefore (as the distal 2 sensors are at/beyond the level of the anal canal) the total recording length within the rectum is likely to be <5cm. The rectal activity recorded is therefore only representative of the most distal rectum and is unlikely to be truly representative of pan-rectal activity.

Additionally, the reporting of perception of gastrointestinal sensations is likely to be subject to a number of biases. Despite efforts from the researcher to put participants at ease, admitting to the urge to pass wind / urge to pass stool is culturally taboo and therefore likely to be reported inconsistently between individuals. Whether co-operation with the request to report sensations was similar between healthy volunteers and patients with faecal incontinence is unknown, however it is possible that this limitation particularly impacted the incontinent group due to the distressing and is the subjective nature of sensation reporting.

It was also noted by the researcher that participants' attention to sensations were influenced by activity. Participants were asked to refrain from engaging in distractions (e.g. in depth conversation, listening to music) to allow attentiveness to the experiment however it is likely that there remained a degree of inattention in some individuals.

Additionally, it should be noted that for reasons of feasibility, patients were allowed to continue medication such as loperamide until the night before the research study. Loperamide in particular is known to reduce rectal sensitivity and colonic transit (Sandhu et al., 1981, Musial et al., 1992). Although the half life of loperamide is 10.8 hours with a range of 9.1 - 14.4 hours with a range of 9.1 - 14.4 hours (MHRA, 2011) it is still conceivable that in the washout period there may have been some impact on measured results.

A significant limitation of this study was the small pilot nature of the study sample. The numbers of patients and volunteers recruited were based on feasibility rather than a formal sample size calculation and for this reason all statistical comparisons should be interpreted with appropriate caution. A post hoc sample size calculation revealed that 55 individuals in each group would be required to formally detect a large effect between groups. Clearly this study is significantly smaller than this.

Furthermore, due to the differences found between healthy male and female TASR characteristics, the decision was made to only compare female healthy volunteers and patients. The conclusions of this therefore may not be applicable to male patients with faecal incontinence. This is particularly pertinent as the underlying causes for faecal incontinence between males and females is thought to be different (Burgell et al., 2012, Townsend et al., 2016).

Finally, it is pertinent to appreciate the limitations associated with the method used for analysis of TASR characteristics. To explore morphological and manometric features of the TASR response, TASRs from all individuals were grouped and analyzed together. This resulted in a dataset with multiple data points from some individuals and few (or none) from others (due to the differing number of TASRs between individuals). It is likely that this has resulted in an element of confounding, as characteristics may be attributable in part to the individual in whom the TASRs were recorded.

It is also noteworthy to report that this study was conducted and analyzed by the same investigator without blinding and it is therefore important to appreciate that reporting bias is a possible feature of data collection and analysis.

7.7.2 Implications of this study

Transient anal sphincter relaxations are a normal physiological occurrence in healthy volunteers and result in a significant reduction in average anal sphincter pressure. A proportion of these are consciously perceived as the urge to pass stool or the urge to pass wind.

In this study, there were no instances in which participants reported the urge to pass wind or stool without the presence of a TASR. It therefore likely that TASRs are a central element in the conscious control of continence. It is appreciated that the physiological control of defaecation is reliant on the coordinated sensory and motor efforts of the colon, rectum and anus. Current opinion is that disordered defaecation is secondary to several disturbances of anorectal and colonic physiology and not purely a sphincter disturbance in patients with FI. This study highlights alteration of TASR characteristics, a recently overlooked feature of anorectal function, which is likely to be a key feature in the maintenance of continence.

This study supports the evolving dataset that supports the role of anal sensory function in the maintenance of continence. Indeed, recent evidence suggests that newly adopted treatments for incontinence such as sacral nerve stimulation and percutaneous tibial nerve stimulation are likely to work via modulation of modify ascending supraspinal control of defaecation (Carrington and Knowles, 2011, Carrington et al., 2014b). Indeed, aecdotal evidence suggests that patients who successfully undergo treatment for faecal incontinence often report the renewed knowledge of 'defaecatory desire'. It is possible that restoration of altered TASR characteristics could be the mechanism for this symptomatic improvement.

Ultimately further studies to more definitively establish TASR characteristics in health and disease are required to further explore the influence of this continence mechanism.

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Chapter 8

8 Discussion: Thesis overview, key findings, further work and conclusions

8.1 Thesis overview

Assessment of pelvic floor control is a fundamental feature of physiological assessment in patients presenting with symptoms of faecal incontinence (FI) and the utility of anorectal manometry (ARM) as a tool for quantifying sphincteric function has long been recognized.

Despite this, there is much debate as to the optimum method of equipment setup, performance technique and results reporting which has resulted in significant dissimilarity amongst practices in both clinical and research settings.

This variation in practice has been further complicated by the recent introduction of a novel method for data collection and interpretation, called high-resolution anorectal manometry (HRAM). This technique employs an increased number of manometric sensors for data collection and displays data with the use of spatiotemporal plots.

This novel technique is significantly more expensive than conventional methods of ARM and little data exists as to its additional (if any) benefits over existing technology.

8.2 Review of thesis aims

The aims of this thesis were to:

(13) Explore existing practices of anorectal manometry
(14) Examine current evidence for the use of HRAM
(15) Develop and validate a protocol for the performance of HRAM
(16) Define normal values for traditional measures of sphincteric function using HRAM
(17) Develop and validate novel measures of sphincteric function, and explore whether they improve diagnostic accuracy in patients with FI
(18) Examine anorectal function over a prolonged period with HRAM to evaluate the phenomenon of anal sampling in both health and patients with FI

8.3 Key findings

8.3.1 Chapter 2 – International survey of methods for anorectal manometry: An exploration of variability in current practice

This was a questionnaire-based study that aimed to examine and compare international practices of anorectal manometry. Questions explored department setup, study indications, manometry technique, study protocol, data analysis and reporting.

The questionnaire was distributed with the assistance of the major neurogastroenterological societies and 62 complete responses from Europe, Asia, America, South America and Australasia were received.

8.3.1.1 Key findings

This study demonstrated

(1) ARM is commonly performed for investigation of patients with constipation, evacuatory dysfunction and faecal incontinence (98% 61/62 or centres surveyed) and is sometimes used for the assessment of sphincter either prior to elective surgery or following obstetric injury.

(2) Fifty-eight percent (52/62) of centres utilise validated symptom severity scores for the pre-procedure assessment of symptomatology.

(3) No centres perform ARM in isolation and all centres reported performing at least 1 further allied study for assessment of both FI and constipation (most commonly rectal sensation to balloon distension (94% 58/62) and/or endoanal ultrasound (60% 37/62).

(4) The majority of centres (35/62 [57%]) perform traditional / conventional anorectal manometry (CAM). Twenty-four centres (24/62 [39%]) reported performing the more novel high resolution or 3D high-resolution manometry (HRAM).

(5) Derivation of normal values was variable between centres with over half (38/62 [61%]) utilizing data from a published study of normal ranges and a quarter (15/62 [24%]) of centres using normal values from a local study of healthy volunteers.

(6) There was marked variation in catheter diameter, sensor number and port configuration between centres. Catheter diameter varied between 8 – 22F for both water-perfused and solid-state systems.

(7) There was marked variation in the manoeuvres performed during ARM and even further variation in the methods for results reporting.

8.3.2 Chapter 3 – Review of high resolution anorectal manometry and its current place in clinical work and in research

This was a systematic review of all clinical papers published in the literature describing the utility of HRAM. The literature search revealed 61 articles, of which 18 were deemed suitable for inclusion. Ten articles described data from 3-dimensional HRAM, 7 from 2-dimensional HRAM and 1 article compared data derived from 2-dimensional and 3-dimensional analysis.

8.3.2.1 Key findings

This systematic review demonstrated:

(1) Four articles exist that compare HRAM with conventional ARM. All studies reported good correlation of values between techniques (interclass correlation coefficients (ICC) ranging from 0.42 – 0.9).

(2) Five articles exist which describe traditional measures of normal anal function in healthy volunteers using HRAM. All studies report the ability to easily demonstrate traditional measures using the HRAM display and some reported that colour contour plots appeared to display findings previously unrecognized with conventional ARM.

(3) Three studies exist that compare three-dimensional HRAM to other allied investigations of anorectal structure and function. These studies demonstrated that there is little utility for 3D-HRAM to predict anatomical abnormalities and that it should be considered complimentary to existing techniques.

(4) Four studies exist that presented data of new methods of analysis to describe anorectal function with HRAM. In particular the use of an integrated pressure volume analysis for evaluation of rectoanal co-ordination may prove a useful adjunct to existing measures of evacuatory function.

8.3.3 Chapter 4 – Development and validation of a standardized protocol for high resolution anorectal manometry

This was a pilot study that aimed to develop and define an optimal investigation protocol for HRAM. Fifty asymptomatic volunteers underwent a prolonged protocol of anorectal function testing to examine the technical assessment of the minimum familiarization period required, optimum resting time and ideal squeeze number.

8.3.3.1 Key findings

This study demonstrated:

(1) A minimum 3-minute familiarisation period is required prior to measurement of anal resting pressure.

(2) A minimum of 2 squeeze manoeuvres is required due to excessive voluntary effort during the first squeeze maneuver in males.

(3) There is no difference in endurance squeeze time between repeat attempts at endurance squeeze

(4) There is no difference in residual push pressure during repeat attempts at push

(5) There is no group difference in anal response to cough during repeat attempts to cough

(6) There is some intra-individual variability in anal response to push and cough which may be clinically relevant and related to volitional effort.

(7) A 30 second between maneuver interval is required to allow resolution / stabilisation of anal pressures prior to further investigation.

8.3.4 Chapter 5 – Traditional measures of normal anorectal function using high resolution anorectal manometry in 140 healthy volunteers

This was a study of anorectal function in 106 females and 34 male healthy volunteers which aimed to establish new normative data sets of an adequate size for recognized measures of anal sphincter function using HRAM.

8.3.4.1 Key findings

This study demonstrated:

(1) Traditional measures of anorectal function can be derived using the HRAM technique.

(2) Some differences in anorectal function exist between males and females with males exhibiting higher mean and maximum absolute squeeze pressures than females.

(3) Some differences in anorectal function exist between parous and nulliparous females with parous females exhibiting lower maximum and incremental squeeze pressures than nulliparous females.

(4) The colour contour plots allowed clear appreciation of anorectal pressure changes during manoeuvres of rest, squeeze, push and cough.

(5) Normal values for traditional measures were defined.

(6) Examination of colour contour plots especially during cough and push provided appreciation of events previously unrecognized with conventional manometry, which may benefit from further investigation.

8.3.5 Chapter 6 – Anal sphincter profiles: development and analysis of a novel instrument for assessment of anal motor function using high resolution anorectal manometry

This was a prospective observational study of 95 female patients with a primary presenting complaint of FI and 85 healthy female volunteers. All participants underwent HRAM. Novel methods of analysis for quantitative assessment of anal rest and squeeze function were compared to derived conventional measures (via data subsampling). The utility of each measure to discriminate between HV and FI groups and correlate with markers of reduced anal sphincter function was assessed and measures compared to establish the optimum instrument for reporting of voluntary anal squeeze.

8.3.5.1 Key findings

This study demonstrated:

(1) For rest, despite demonstrating a lower sensitivity than the other high resolution measures of anal sphincter function (27% HRAM-RP vs. 35% HRAM-RA), the HRAM-RA showed the greatest curve area during ROC analysis for detecting abnormal function in symptomatic individuals.

(1) For squeeze, the HRAM-SP-5 was shown to have markedly improved sensitivity for detecting abnormal sphincter function in patients with FI (59%) when compared to CAM-SI (36%)

(2) The negative correlation between HRAM-RP and HRAM-SP-5 measures and symptom severity was markedly stronger for than conventional measures however improvement was more modest for description of rest than voluntary squeeze.

(3) HRAM-SP-5 scores were reduced in those patients with sphincter abnormalities when compared to patients with intact anal sphincter anatomy.

(4) HRAM-SP-5 identified 25 previously unrecognized patients (26%) with impaired sphincter function. This group reported similar symptom severities to the group as a whole.

8.3.6 Chapter 7 – Characteristics of transient anal sphincter relaxations: a prolonged study of anorectal function in health and faecal incontinence using high resolution anorectal manometry

This was a pilot study of prolonged anorectal motor function using HRAM in 27 healthy volunteers and 19 patients with FI. The study aimed to characterise transient anal sphincter relaxations (TASRs) and to examine differences in morphology and frequency in health and disease. In particular, the impact of a high fat meal and the association of events with conscious perception were explored.

8.3.6.1 Key findings

In health this study demonstrated:

(1) TASRs were an uncommon event preprandially in heathy volunteers (median preprandial TASR count of 1 in the 45-minute preprandial period). TASR frequency significantly increased following meal consumption (median postprandial TASR count of 3 in the 45-minute preprandial period).

(2) TASRs typically lasted 25 seconds and involved 53% of the anal canal length. They were associated with a 40% reduction in average anal sphincter pressure.

(3) TASRs appeared to be associated with a small but significant increase in rectal pressure (median 7mmHg change).

(4) TASRs appeared to involve a greater absolute length of the anal canal, and resulted in a greater percentage drop in sphincter pressures in females when compared to males.

(5) Approximately half (97/207 [47%]) of the TASRs recorded were perceived by one individual, most commonly as the urge to pass wind (66/97 [32%]).

(6) Perceived TASRs involved a greater percentage length of the anal canal than non-perceived TASRs.

When comparing female patients with FI to female healthy volunteers this study demonstrated:

(1) In females with FI, TASRs appeared to occur more infrequently at baseline than in healthy volunteers and were only seen in 2/10 (20%) of FI subjects studied.

(2) There appeared to be little change in TASR count following meal consumption in females with FI (median post-prandial TASR count of 0.5 in FI vs. 3 in HV).

(3) TASRs appeared to involve a smaller percentage anal canal length in females with FI and were associated with a smaller percentage change in anal sphincter pressure.

(4) TASRs were rarely perceived (only perceived by a single patient studied).

(5) Two patients with FI were found to have a significant and prolonged postprandial drop in anal pressure that was not perceived.

8.4 Future studies

The studies contained within this thesis have demonstrated the variability of current practices and have established a robust protocol for the practice of HRAM.

A novel method of analysis has been demonstrated to have improved utility for the quantification of sphincter function when compared with existing techniques.

In addition the physiological studies in healthy volunteers and patients with faecal incontinence has expanded our knowledge of anorectal function and has given insight into the mechanisms underlying faecal continence. However, further research is required to determine the impact of variations in manometric equipment and the study protocol on quantitative values of anorectal function.

The questionnaire presented in Chapter 2 has demonstrated significant variation in the practice of anorectal manometry internationally.

On the basis of a small amount of literature (most predominantly from examination of the oesophagus) there is a general assumption that features such as catheter diameter and perfusion rates affect quantitative values. Although this is likely to be the case the clinical significance of this has not yet been demonstrated.

This is a particularly pertinent question, because such differences are often used as the reason for variation from current guidelines. Demonstration of the impact of equipment setup would provide clinicians and researchers with the necessary baseline information required prior to effective technique standardization.

An adequately powered comparative study of anorectal manometry performed in either patients or healthy volunteers with alternate equipment would provide the information to answer this question.

What is the additional benefit of 3-dimensional HRAM?

This thesis focused on the development and standardization of two-dimensional HRAM. However it is appreciated that there is a sizable body of literature pertaining to vector volume manometry that demonstrates an association between sphincter asymmetry and impaired continence. Indeed, the literature review outlined in chapter 3 highlighted a number of articles that further explored three-dimensional function of the anal canal utilizing 3D HRAM.

Although the knowledge that pressure within the anal canal is asymmetrical is not novel, the increased resolution that a 256-channel manometry catheter delivers could provide further insight into the functional morphology of the sphincter. In particular, it is conceivable that 3D application the 'profile' of analysis could provide an even more accurate description of anal function and this is an area that warrants further investigation.

What is the additional clinical utility of the newly developed HRAM 5-second profile measure?

The data presented in Chapter 6 has demonstrated that the HRAM profile measures are superior to CAM measures of rest and squeeze with increased sensitivity for detection of poor sphincter function and better correlation with symptom severity.

The question of the utility of this measure remains. Two particular areas of interest would be useful targets for future research.

First is the usefulness of the HRAM-SP-5 as a biomarker for treatment stratification. If the novel measure is found to be more discriminatory than existing measures, it could have the potential for improving outcomes in those whose management may previously have been misdirected. A prospective case series of anal sphincter function as described using the HRAM-SP-5 before and after intervention would be an appropriate initial step. Should differences be seen, a further randomized blinded study of intervention on the baseline HRAM-SP-5 scores would provide more definitive information as to the utility for predicting response to treatment.

A separate but allied question is whether HRAM profile scores could be used to examine changes in sphincter function following intervention. This measure could have potential use for treatment monitoring and may act as an objective marker in a field which is notorious for treatments which harbor a significant placebo effect.

Can the increased spatiotemporal resolution afforded by HRAM provide further metrics to better describe anal sphincter function?

The study of traditional measures in Chapter 5 provided the opportunity to qualitatively review a series of colour contour images of anal function in healthy volunteers. This provided appreciation of events previously unrecognized with conventional manometry such as the relative relaxation of the anal canal following cough and the heterogeneity of sphincter recruitment during squeeze.

Further comparison of specific features of function in health and patient groups, as was performed with the novel profile measures in Chapter 6 may reveal further metrics to better define sphincter function.

What are the mechanisms underlying TASR generation?

Chapter 7 of this thesis suggests that TASRs are likely to be an important feature underlying the normal call to stool and that this mechanism may be disrupted in some patients with faecal incontinence. There are 2 particular issues with regard to TASR characteristics, which deserve further attention. The first is to further elucidate whether TASRs are entirely smooth muscle (i.e. IAS) generated. This could be performed with electromyographical studies of the internal sphincter, external sphincter and puborectalis. The second would be to perform a control study by blocking nitric oxide receptors in the anal canal, to see the effect on TASR frequency and morphology. Also with the recent application of the endoflip device, it would be interesting to relate anal opening pressures to TASR features.

What is the role of the transient anal sphincter relaxation in the maintenance of continence?

The initial pilot data from Chapter 7 has suggested that TASRs may be an important feature in the maintenance of continence. Due to the small study sample size few conclusions about TASR characteristics and an accurate assessment of these characteristics cannot be drawn.

Further adequately powered studies examining prolonged anal function and anorectal sensory perception in patients with FI (particularly before and after an intervention thought to impact sensation such as SNS / PTNS or sensory biofeedback) would more clearly define the features of this proposed continence mechanism.

8.5 Conclusions

Anorectal manometry is a commonly performed investigation for the assessment of patients with symptoms of disordered defaecation. Unfortunately, despite the attempts of working parties, performance of this investigation is poorly standardized.

High-resolution manometry within the anal canal is characterised by closer sensor spacing and display of data in a spatiotemporal plot. Data that demonstrate the additional benefits of HRAM over conventional manometry are emerging; however there are currently remain few published studies on the technique.

Exploration of HRAM data in health and in patients with FI has revealed a novel method of reporting more global anal sphincter function – the 'profile' rest and 'squeeze' pressures. Further analysis in the utility of these and other descriptives of global anal function may well improve diagnostic utility of this technique.

Ultimately, HRAM will only become a clinically useful investigation if standardization of the technique is promoted so that protocols are comparable. This would allow results to be transferrable between institutions. Such consensus is called for so as to avoid the pitfalls that have affected conventional manometry (and all other tests of anorectal function).

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Appendix A

International Anorectal Physiology Working Group

Department setup

Dear Colleague

Thank you very much for taking the time to complete this questionnaire

The aim of this project is to explore variations in the current practice of anorectal manometry and the questionnaire asks about indications for investigation, catheter set up and results reporting

This process is part of the International Working Group for Gastrointestinal Motility and Function and has the support of has been supported by a number of societies including the ESMN, ANGMA, ANMA, UEG, ESCP and ANMS.

Completion should take less than 15 minutes to complete and it is hoped that results will provide an initial step towards standardisation of this, and other investigations of anorectal function

We greatly appreciate your time and effort

Dr Emma Carrington
Senior Research Fellow

Dr Mark Scott
Senior Clinical Scientist

Professor Charles Knowles
Professor of Surgical Research

Professor Mark Scott
Professor of Gastroenterology

Steering Committee
International Anorectal Physiology Working Group (IAPWG)

International GI Motility and Function Working Group

ESNM European Society of Neurogastroenterology & Motility · ANGMA · ANMA · in association with United European Gastroenterology ueg · ESCP

July 2014

Section 1 - Department setup and basic information

What is the name of your institution?

In what type of institution is your department based?

- ◯ Department within a specialist hospital
- ◯ Department within a general hospital
- ◯ Department within a primary care centre
- ◯ Department within a private clinic / hospital

Other

You answered 'other' to the last question (in what type of institution is your department based)

Please provide more information below

In what country is your institution based?

Approximately how many studies are performed in your institution each year?

- < 50 (less than 1 per week)
- 50 - 100 (1 - 2 per week)
- 100 - 200 (2 - 4 per week)
- 200 - 500 (4 - 10 per week)
- 500 - 1000 (10 - 20 per week)
- > 1000 (more than 20 per week)

Study indications

Section 2 - Study indications

In your department, how often is anorectal manometry performed for the following indications?

	Never	Sometimes	Often
Faecal urgency			
Urge faecal incontinence			
Passive faecal incontinence			
Post defaecatory leakage			
Flatus incontinence			
Evacuatory difficulty			
Constipation			
Anal pain			
Abdominal pain / bloating			
Pre operative sphincter assessment			
Post obstetric injury sphincter assessment			

Pre-study assessment

Section 3 - Pre study assessment

Are validated symptom scores used as part of your assessment?

- Yes
- No

Which of the following scoring systems are used to assess symptoms of faecal incontinence?

Please select all that apply

- ☐ Wexner score
- ☐ Vaizey score
- ☐ Pescatori score
- ☐ American Medical Systems score
- ☐ The Douglas Wong score
- ☐ Other

You answered 'other' to the last question

Please provide more information below

Which of the following scoring systems are used to assess symptoms of constipation?

- ☐ Cleveland Clinic constipation score
- ☐ KESS
- ☐ PAC-SYM
- ☐ Obstructive Defaecation Score (ODS)
- ☐ Constipation Assessment Score
- ☐ Other

You selected 'other' to the last question

Please provide more information below

Is quality of life assessed?

- ◯ Yes
- ◯ No

Which of the following methods do you use assess quality of life?

- ☐ Rockwood FI QoL
- ☐ GI QoL questionnaire
- ☐ PAC QoL
- ☐ SF- 36
- ☐ Informal assessment
- ☐ Other

You selected 'other' to the last question

Please provide more information below

Is a clinical examination performed prior to anorectal physiology?

- Yes
- No

What does this clinical examination include?

Please select all that apply

	Never	Sometimes	Routinely
Inspection of the perineum			
Inspection during straining			
Digital rectal examination (DRE)			
DRE during squeeze			
DRE during straining			
DRE during cough			
Proctoscopy			
Rigid sigmoidoscopy			
Vaginal examination			

Manometry technique and background

Section 5 - Basic equipment and protocol considerations

What type of anal manometry is performed in your department?

If more than one technique is used, please choose the technique **most commonly** performed

- Traditional manometry
- Vector volume manometry
- High resolution manometry
- 3D high resolution manometry
- High definition manometry

What units do you use to report results?

- cmH_20
- mmHg

What type of catheter is used?

- Water perfused
- Solid state

What technique do you use to perform your studies?

- Station / manual pull through
- Stationary
- Automatic pull through

What measurement system do you routinely use?

If more than one system, please choose the one **most commonly** used

- MMS (Solar)
- Given (ManoScan)
- Sandhill (InSIGHT)
- Albyn (SmartGI)
- Laborie
- Medspira (mcompass / Encompass)
- Arndorfer Medical Specialties
- Other

You ansered 'other' to the last question

Please provide more information below

How did your department derive normal values for anal manometry?

- Local study of healthy volunteers
- Published study of normal ranges
- No formalised normal range used
- Other
- Not sure

You answered 'other' to the last question

Please provide more information below

How large was the sample size in your local study of healthy volunteers?

- <10 volunteers
- 10 - 20 volunteers
- 20 - 40 volunteers
- 40 - 60 volunteers
- 60 - 100 volunteers
- > 100 volunteers

During your local study of healthy volunteers, was the equipment set up and study protocol identical to the one used at present?

- Yes
- No
- Not sure

Was the equipment set up and study protocol in the published study of normal ranges identical to the one used within your department?

- Yes

- ◯ No
- ◯ Not sure

Water perfused catheter specifications

Section 6 - catheter description (water perfused)

How many perfusion channels does your manometry catheter have?

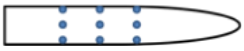
1	2 - 4	5 - 8	9 - 12	>12	I'm not sure
◯	◯	◯	◯	◯	◯

How are these perfusion channels arranged?

◯  longitudinally

◯  spirally

◯  radially

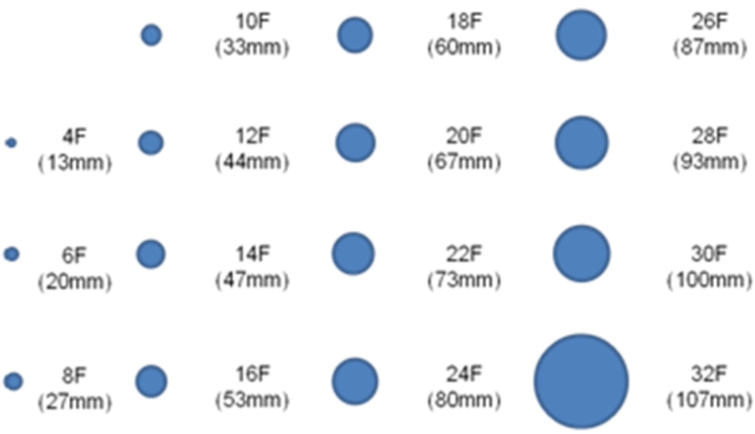
◯  longitudinally and radially

◯ I'm not sure

Use the slider below to indicate the <u>total recording length</u> of these channels

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
longitudinal length (cm)																

Please click on the circle that best describes the diameter of the catheter you use



I'm not sure

Solid state catether specifications

Section 6 - catheter description (solid state)

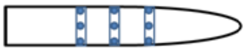
How many sensors does your manometry catheter have?

1	2 - 4	5 - 8	9 - 12	13 - 20	21 - 40	> 40	I'm not sure
○	○	○	○	○	○	○	○

How are these sensors arranged?

○  longitudinally

○  radially

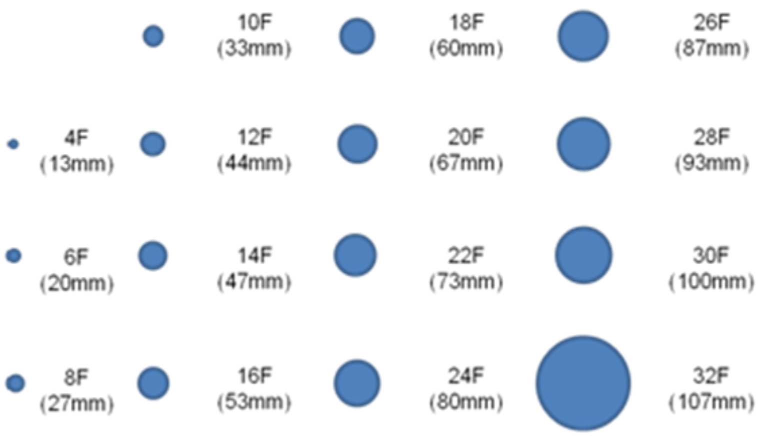
○  longitudinally and radially

○ I'm not sure

Use the slider below to indicate the total recording length of these sensors

	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10
longitudinal length (cm)																					

Please click on the circle that best describes the diameter of the catheter you use



I'm not sure

Study protocol

Section 7 - study protocol

During anal manometry, what tests / manoeuvres are performed for investigation of **faecal incontinence**?

	Not performed	Routinely performed
Anal resting pressure	○	○
Anal squeeze pressure	○	○

Prolonged anal squeeze / squeeze duration	◯	◯
Cough / involuntary squeeze	◯	◯
Attempted defaecation / push	◯	◯
Recto-anal inhibitory reflex (RAIR)	◯	◯

During anal manometry, what tests / manoeuvres are performed for investigation of **constipation**?

	Not performed	Routinely performed
Anal resting pressure	◯	◯
Anal squeeze pressure	◯	◯
Prolonged anal squeeze / squeeze duration	◯	◯
Cough / involuntary squeeze	◯	◯
Attempted defaecation / push	◯	◯
Recto-anal inhibitory reflex (RAIR)	◯	◯

After insertion of the catheter, but before tests begin, do you allow for a period of familiarisation?

◯ Yes

◯ No

Use the sliding bar below to indicate the length of this familiarisation period in minutes

	0	1	2	3	4	5	6	7	8	9	10
time (minutes)											

Anal resting pressure

During assessment of anal resting pressure, is the patient asked to rest for a pre-defined length of time?

◯ Yes

◯ No, the resting time is variable

Use the sliding bar below to indicate the length of time given to record anal resting pressure

	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
anal resting pressure time (minutes)											

Which of the following parameters are used to report anal resting pressure?

Please select all that apply

☐ Mean pressure at different levels of the anal canal

☐ Mean pressure over the whole anal canal

- Maximum pressure at different levels of the anal canal
- Maximum pressure over the whole anal canal
- Other

Do you report resting symmetry ?

Never	Sometimes	Routinely
○	○	○

How is resting symmetry reported?

Please select all that apply

- Quantitatively using the in-built analysis software
- Quantitatively deriving values manually from line traces
- Qualitatively from the colour-contour images

You answered 'other' to the last question

Please provide more information below

Anal squeeze pressure

During assessment of voluntary squeeze, is the patient asked to squeeze for a pre-defined length of time?

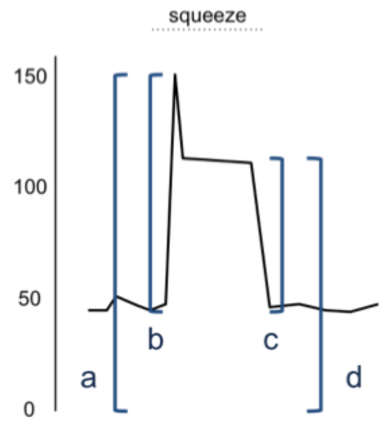
- Yes
- No, the patient squeezes for as long as they are able

Use the sliding bar below to indicate the length of time in which the patient is asked to sustain a voluntary squeeze

	0	5	10	15	20	25	30	35	40
Time of squeeze (seconds)									

Which of the following do you report during assessment of anal squeeze?

Please select all that apply



- [ ] a (maximum absolute squeeze pressure)
- [ ] b (maximum incremental squeeze pressure)
- [ ] c (sustained incremental squeeze pressure)
- [ ] d (sustained absolute squeeze pressure)
- [ ] other

You answered 'other' to the previous question

Please provide more information below

How do you report anal squeeze pressures with the high resolution system?

Please select all that apply

- [ ] Quantitatively using the in-built analysis software
- [ ] Quantitatively deriving values manually from line traces
- [ ] Qualitatively from the colour-contour images

Do you report squeeze symmetry ?

Never	Sometimes	Routinely
○	○	○

How is squeeze symmetry reported?

Please select all that apply

- [ ] Quantitatively using the in-built analysis software
- [ ] Quantitatively deriving values manually from line traces
- [ ] Qualitatively from the colour-contour images

Use the sliding bar below to indicate the number of voluntary squeezes performed

	0	1	2	3	4	5	6	7	8	9	10
number of squeezes performed											

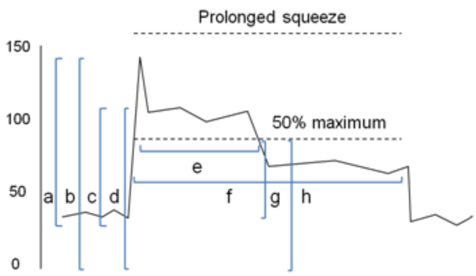
Prolonged anal squeeze / squeeze duration

Use the sliding bar below to indicate the length of time in which the patient is asked to sustain a voluntary <u>sustained</u> squeeze

	0	5	10	15	20	25	30	35	40	45	50	55	60
Time of sustained squeeze (seconds)													

What parameters are reported for prolonged anal squeeze / squeeze duration?

please select all that apply



- ☐ a (maximum incremental pressure)
- ☐ b (maximum absolute pressure)
- ☐ c (incremental sustained pressure)
- ☐ d (incremental absolute pressure)
- ☐ e (duration of squeeze above 50% maximum pressure)
- ☐ f (duration of squeeze above resting pressure)
- ☐ g (incremental pressure at 50% maximum)
- ☐ h (absolute pressure at 50% maximum)
- ☐ Other

You answered 'other' to the previous question

Please provide more information below

How do you report prolonged anal squeeze pressures with the high resolution system?

Please select all that apply

- ☐ Quantitatively using the in-built analysis software
- ☐ Quantitatively deriving values manually from line traces
- ☐ Qualitatively from the colour-contour images

Do you report prolonged squeeze symmetry ?

Never	Sometimes	Routinely
○	○	○

How is prolonged squeeze symmetry reported?

Please select all that apply

- ☐ Quantitatively using the in-built analysis software
- ☐ Quantitatively deriving values manually from line traces
- ☐ Qualitatively from the colour-contour images

Use the slider below to indicate the number of prolonged anal squeezes performed during each study

	0	1	2	3	4	5	6	7	8	9	10
number of prolonged squeezes recorded											

Cough / involuntary squeeze

During the cough manoeuvre, do you measure both rectal and anal pressures?

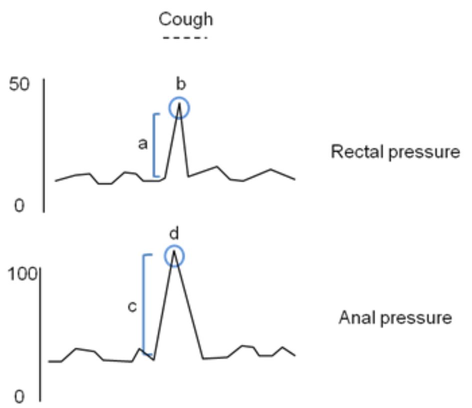
- ◯ Yes, we measure both rectal and anal pressures
- ◯ No, anal pressures only
- ◯ No, rectal pressures only
- ◯ Neither rectal or anal pressures are measured

How do you report the results of the cough manoeuvre?

Please select all that apply

- ☐ Quantitatively using the in-built software
- ☐ Quantitatively deriving values manually from line traces
- ☐ Qualitatively using the colour-contour images
- ☐ The manometric results of this test are not reported i.e. only visualisation of appropriate muscle recruitment / co-ordination is reported

What values do you report? Please select all that apply



- ☐ a (change in rectal pressure during cough)
- ☐ b (maximum rectal pressure during cough)
- ☐ c (change in anal pressure during cough)
- ☐ d (maximum anal pressure during cough)

- [ ] c - a (subtract pressure a from pressure c) = anorectal pressure difference during cough
- [ ] Other
- [ ] Quantitative values are not reported

You answered 'other' to the previous question

Please provide more information below

Do you report symmetry of the anal cough response?

Never	Sometimes	Routinely
○	○	○

How is the symmetry of the anal cough reponse reported?

Please select all that apply

- [ ] Quantitatively using the in-built analysis software
- [ ] Quantitatively deriving values manually from line traces
- [ ] Qualitatively from the colour-contour images

Use the slider below to indicate the number of coughs recoded during each study

	0	1	2	3	4	5	6	7	8	9	10
Number of coughs recorded											

Attempted defaecation / push

How is the patient positioned during the manoeuvre?

Please select all that apply

- [ ] Supine
- [ ] Left lateral
- [ ] Sitting on a commode
- [ ] Other

During the attempted defaecation / push manoeuvre, is a balloon placed in the rectum?

- ○ Yes
- ○ No

To what amount is the balloon filled?

- ○ A pre-defined, fixed amount
- ○ The patient's first sensory volume
- ○ The patient's defaecatory desire volume

Use the slider below to indicate the fixed balloon volume used during the manoeuvre

	0	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	160
Balloon volume (mls)																	

During the attempted defaecation / push manoeuvre do you measure both rectal and anal pressures?

- Yes, we measure both rectal and anal pressures
- No, anal pressures only
- No, rectal pressures only
- Neither rectal or anal pressures are measured

How do you report the results of attempted defaecation / push

Please select all that apply

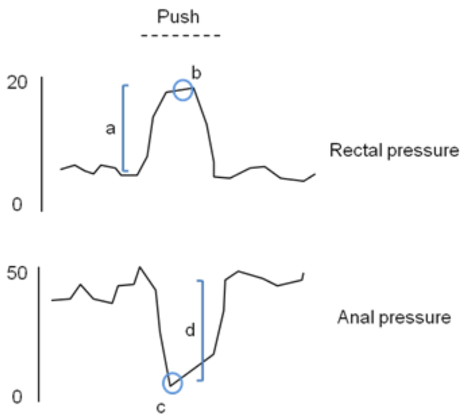
- Quantitatively using in-built analysis software
- Quantitatively deriving values manually from line traces
- Qualitatively from colour contour / line traces
- The manometric results of this test are not reported i.e. only visualisation of appropriate muscle recruitment / co-ordination is reported

How do you report the results of attempted defaecation / push

Please select all that apply

- Quantitatively using in-built analysis software
- Quantitatively deriving values manually from line traces
- The manometric results of this test are not reported i.e. only visualisation of appropriate muscle recruitment / co-ordination is reported

What values do you report? Please select all that apply



- a (change in rectal pressure during push)
- b (rectal pressure during push)
- c (minimum anal pressure during push)
- d (change in anal pressure during push)
- Push percentage (percentage fall in anal pressure from baseline)
- Rectoanal gradient

- [ ] Other
- [ ] Quantitative values are not reported

You answered 'other' to the previous question

Please provide more information below

Do you report push symmetry?

Never	Sometimes	Routinely
○	○	○

How is push symmetry reported?

Please select all that apply

- [ ] Quantitatively using the in-built analysis software
- [ ] Quantitatively deriving values manually from line traces
- [ ] Qualitatively from the colour-contour images

Use the slider below to indicate the number of attempted defaecation / push manoeuvres performed in each study

	0	1	2	3	4	5	6	7	8	9	10
Number of push manoeuvres											

Recto-anal inhibitory reflex / RAIR

How do you provoke a RAIR?

- ○ Inflation of the rectal balloon with a single fixed volume of air
- ○ Incremental inflation of the rectal balloon with fixed volumes of air until a RAIR is seen
- ○ Other

You answered 'other' to the previous question

Please provide more information below

Use the slider below to indicate the fixed volume of air / water used

	0	20	40	60	80	100	120	140	160	180	200
balloon volume (mls)											

Use the slider below to indicate the initial fixed volume of air / water used

	0	10	20	30	40	50	60	70	80	90	100
balloon volume (mls)											

Use the slider below to indicate subsequent incremental volumes used until a RAIR is visualised

	0	10	20	30	40	50	60	70	80	90	100
incremental volume (mls)											

How is the RAIR reported?

Please select all that apply

- ☐ Quantitatively (volume required to elicit response)
- ☐ Qualitatively (present / absent)

Use the slider below to indicate the number of RAIRs performed in each study

	0	1	2	3	4	5	6	7	8	9	10
Number of RAIRs performed											

Additional investigations, data analysis and reporting

Section 8 - Additional investigations, data analysis and reporting

In addition to anal manometry, how often are the following tests performed for the investigation of faecal incontinence?

	Not performed	Sometimes	Routinely performed
Rectal sensation (balloon distension)	○	○	○
Rectal sensation (electrical stimulation)	○	○	○
Rectal sensation / compliance (barostat)	○	○	○
Anal sensation (electrical stimulation)	○	○	○
Pudendal nerve function (terminal motor latencies)	○	○	○
Anal endosonography (endoanal ultrasound)	○	○	○
Anal electromyography	○	○	○
Saline continence test	○	○	○
Balloon expulsion	○	○	○

Evacuation proctography	○	○	○
Colonic transit	○	○	○
Colonic scintigraphy	○	○	○

If you routinely perform other tests for the investigation of faecal incontinence please provide more information below

In addition to anal manometry, how often are the following tests performed for the investigation of constipation?

	Not performed	Sometimes	Routinely performed
Rectal sensation (balloon distension)	○	○	○
Rectal sensation (electrical stimulation)	○	○	○
Rectal sensation / compliance (barostat)	○	○	○
Anal sensation (electrical stimulation)	○	○	○
Pudendal nerve function (terminal motor latencies)	○	○	○
Anal endosonography (endoanal ultrasound)	○	○	○
Anal electromyography	○	○	○
Saline continence test	○	○	○
Balloon expulsion	○	○	○
Evacuation proctography	○	○	○
Colonic transit	○	○	○
Colonic scintigraphy	○	○	○

If you routinely perform other tests for the investigation of constipation please provide more information below

End of survey

You have come to the end of this survey.

Once again thank you for your time and effort.

If you have any queries or feedback about this questionnaire please get in touch using the details below.

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London, UK

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Appendix B - data

CHAPTER 4 - DEVELOPMENT AND VALIDATION OF A STANDARDISED PROTOCOL FOR HIGH RESOLUTION ANAL MANOMETRY

ID	sex	age	parity	R1mean	R1ACL	R1ACPPMe	R1_profile	R2mean	R2ACL	R2ACPPMe
WPSS1002HV	1	36	3	84	3.4	63	214.2	81	3.4	57
WPSS1006HV	2	23	0	95	3.3	63	207.9	81	3.3	55
ASF1001HV	2	33	0	83	3.7	51	188.7	79	3.7	51
ASF1002HV	2	54	1	61	2.4	42	100.8	52	2.4	33
ASF1003HV	2	31	0	63	3.3	44	145.2	63	3.3	44
ASF1004HV	1	21	3	95	3.9	61	237.9	85	3.9	55
ASF1005HV	2	35	1	55	3.5	34	119	54	3.5	33
ASF1007HV	1	25	3	43	3.7	26	96.2	38	3.6	23
ASF1010HV	1	49	3	115	4.8	73	350.4	132	4.8	84
ASF1013HV	2	47	1	86	3.3	63	207.9	85	3.3	63
ASF1014HV	2	35	1	61	2.6	45	117	56	2.6	40
ASF1016HV	2	48	0	80	2.9	54	156.6	76	2.9	51
ASF1017HV	2	46	1	76	2.9	55	159.5	76	2.9	54
ASF1019HV	2	40	1	64	3.7	46	170.2	65	3.7	45
ASF1021HV	2	44	1	81	5.4	53	286.2	79	5.4	47
ASF1022HV	2	64	1	74	3.6	48	172.8	61	3.6	42
ASF1024HV	2	49	1	109	3.9	82	319.8	102	3.9	79
ASF1025HV	2	41	1	83	5.2	60	312	89	5.2	63
ASF1026HV	2	30	1	89	3.8	55	209	84	3.8	52
ASF1027HV	1	63	3	66	3.2	42	134.4	54	3.2	34
ASF1029HV	1	31	3	98	4.5	40	180	84	4.5	35
ASF1030HV	2	22	0	83	3.5	60	210	70	3.5	54
ASF1031HV	1	21	3	96	3.8	60	228	87	3.8	55
ASF1032HV	2	33	1	70	3.5	49	171.5	59	3.5	43
ASF1033HV	2	37	0	127	3.8	90	342	114	3.8	78
ASF1037HV	2	45	1	74	4	55	220	79	4	57
WPSS1040HV	2	50	1	151	3.9	105	409.5	97	3.9	71
WPSS1034HV	1	47	3	43	4.8	27	129.6	49	4.8	29
WPSS1032HV	2	45	1	89	4.2	50	210	100	4.2	57
WPSS1031HV	2	25	0	91	3.6	57	205.2	74	3.6	49
WPSS1030HV	2	63	1	67	4.1	50	205	79	4.1	55
WPSS1029HV	1	21	3	115	5.3	68	360.4	164	5.3	85
WPSS1028HV	2	23	0	69	4.4	48	211.2	60	4.4	41
WPSS1027HV	2	31	1	105	4.4	68	299.2	110	4.4	71
WPSS1026HV	2	35	1	74	4.5	51	229.5	76	4.5	52
WPSS1025HV	2	57	1	112	2.8	82	229.6	93	2.8	70
WPSS1023HV	2	57	0	145	3.5	86	301	92	3.5	58
WPSS1022HV	2	35	1	61	2.8	45	126	49	2.8	37
WPSS1020HV	2	68	0	90	3.6	57	205.2	66	3.6	49
WPSS1018HV	2	65	0	123	3.6	73	262.8	120	3.6	69
WPSS1017HV	2	23	0	81	3.6	47	169.2	90	3.6	52
WPSS1016HV	2	36	0	99	4.6	65	299	107	4.6	70
WPSS1015HV	2	61	0	84	5.3	62	328.6	78	5.3	54
WPSS1014HV	2	53	1	83	5.3	52	275.6	80	5.3	50
HRAM1033HV	2	41	0	68	3.8	52	197.6	65	3.8	49
HRAM1034HV	2	25	0	102	3.1	71	220.1	100	3.1	65
WPSS1041HV	1	33	3	106	4.6	63	289.8	83	4.6	56
WPSS1043HV	2	51	1	56	4.1	42	172.2	48	4.1	37
WPSS1044HV	1	25	3	121	4.9	78	382.2	112	4.9	73
WPSS1045HV	2	44	0	57	3.1	39	120.9	60	3.1	38

ID	R2_profile	R3mean	R3ACL	R3ACPPMe	R3_profile	R4mean	R4ACL	R4ACPPMe
WPSS1002HV	193.8	72	3.4	50	170	67	3.4	47
WPSS1006HV	181.5	75	3.3	49	161.7	71	3.3	48
ASF1001HV	188.7	81	3.7	49	181.3	75	3.7	45
ASF1002HV	79.2	48	2.4	30	72	49	2.4	32
ASF1003HV	145.2	57	3.3	40	132	57	3.3	40
ASF1004HV	214.5	84	3.6	55	198	81	3.6	52
ASF1005HV	115.5	57	3.5	37	129.5	58	3.5	41
ASF1007HV	82.8	36	3.6	22	79.2	36	3.6	23
ASF1010HV	403.2	153	4.8	83	398.4	128	4.8	77
ASF1013HV	207.9	83	3.3	61	201.3	83	3.3	61
ASF1014HV	104	54	2.6	39	101.4	50	2.6	37
ASF1016HV	147.9	75	2.9	49	142.1	77	2.9	47
ASF1017HV	156.6	74	2.9	54	156.6	73	2.9	53
ASF1019HV	166.5	54	3.4	41	139.4	45	3.4	35
ASF1021HV	253.8	74	5.4	43	232.2	72	5.4	42
ASF1022HV	151.2	68	3.6	41	147.6	70	3.6	41
ASF1024HV	308.1	104	3.9	77	300.3	99	3.9	76
ASF1025HV	327.6	87	5.6	58	324.8	85	5.6	58
ASF1026HV	197.6	79	3.8	49	186.2	77	3.8	48
ASF1027HV	108.8	45	3.2	30	96	42	3.2	28
ASF1029HV	157.5	74	3.1	41	127.1	76	3.1	42
ASF1030HV	189	71	3.2	55	176	70	3.2	54
ASF1031HV	209	86	3.8	55	209	76	3.8	51
ASF1032HV	150.5	65	3.5	49	171.5	65	3.5	49
ASF1033HV	296.4	118	3.8	78	296.4	110	3.8	72
ASF1037HV	228	75	4	55	220	72	4	53
WPSS1040HV	276.9	95	3.9	73	284.7	97	3.9	72
WPSS1034HV	139.2	51	4.8	31	148.8	48	4.8	30
WPSS1032HV	239.4	97	4.2	59	247.8	93	4.2	59
WPSS1031HV	176.4	69	3.6	45	162	68	3.8	42
WPSS1030HV	225.5	75	4.1	52	213.2	74	4.1	50
WPSS1029HV	450.5	132	5.3	74	392.2	140	5.3	79
WPSS1028HV	180.4	60	4.4	40	176	60	4.4	40
WPSS1027HV	312.4	106	4.4	65	286	103	4.4	61
WPSS1026HV	234	79	4.5	54	243	61	4.5	43
WPSS1025HV	196	82	2.8	63	176.4	70	2.8	54
WPSS1023HV	203	88	3.5	56	196	63	3.5	47
WPSS1022HV	103.6	43	2.8	33	92.4	40	2.8	30
WPSS1020HV	176.4	60	3.6	45	162	59	3.6	44
WPSS1018HV	248.4	118	3.6	65	234	114	3.6	61
WPSS1017HV	187.2	80	3.6	47	169.2	88	3.6	48
WPSS1016HV	322	89	4.6	61	280.6	81	4.6	54
WPSS1015HV	286.2	74	5.3	49	259.7	76	5.3	48
WPSS1014HV	265	77	5.3	46	243.8	77	5.3	46
HRAM1033HV	186.2	62	3.7	45	166.5	62	3.7	45
HRAM1034HV	201.5	91	3.1	61	189.1	85	3.1	56
WPSS1041HV	257.6	73	4.6	53	243.8	67	4.5	49
WPSS1043HV	151.7	48	4.1	37	151.7	46	4.1	34
WPSS1044HV	357.7	109	4.9	70	343	105	4.8	70
WPSS1045HV	117.8	59	3.1	37	114.7	62	3.1	37

ID	R4_profile	R5mean	R5ACL	R5ACPPMe	R5_profile	R6mean	R6ACL	R6ACPPMe
WPSS1002HV	159.8	65	3	46	138	64	3.4	45
WPSS1006HV	158.4	62	3	41	123	61	3.3	41
ASF1001HV	166.5	80	4	49	196	70	3.7	45
ASF1002HV	76.8	52	2	34	68	56	2.4	38
ASF1003HV	132	59	3	41	123	53	3.3	38
ASF1004HV	187.2	85	4	54	216	80	3.6	51
ASF1005HV	143.5	57	4	39	156	58	3.5	41
ASF1007HV	82.8	39	4	24	96	39	3.6	24
ASF1010HV	369.6	150	5	78	390	111	4.8	69
ASF1013HV	201.3	78	3	57	171	78	3.3	56
ASF1014HV	96.2	53	3	39	117	49	3	36
ASF1016HV	136.3	75	3	47	141	70	2.9	41
ASF1017HV	153.7	72	3	51	153	69	2.9	48
ASF1019HV	119	39	3	30	90	50	3.4	35
ASF1021HV	226.8	71	5	41	205	70	5.4	41
ASF1022HV	147.6	72	4	40	160	68	3.6	35
ASF1024HV	296.4	91	4	73	292	94	3.9	72
ASF1025HV	324.8	82	6	56	336	77	5.6	53
ASF1026HV	182.4	77	4	49	196	75	3.8	47
ASF1027HV	89.6	40	3	27	81	37	3.2	25
ASF1029HV	130.2	60	3	33	99	52	3.1	29
ASF1030HV	172.8	71	3	52	156	69	3.4	51
ASF1031HV	193.8	73	4	50	200	74	3.8	50
ASF1032HV	171.5	56	4	42	168	53	3.5	39
ASF1033HV	273.6	113	4	73	292	104	3.8	66
ASF1037HV	212	71	4	52	208	67	4	49
WPSS1040HV	280.8	101	4	71	284	100	3.9	68
WPSS1034HV	144	49	5	30	150	46	4.8	28
WPSS1032HV	247.8	103	4	62	248	95	4.2	60
WPSS1031HV	159.6	68	4	41	164	70	3.8	41
WPSS1030HV	205	74	4	49	196	76	4.1	48
WPSS1029HV	418.7	133	5	75	375	144	5.3	77
WPSS1028HV	176	59	4	40	160	60	4.4	40
WPSS1027HV	268.4	100	4	61	244	97	4.1	59
WPSS1026HV	193.5	60	5	42	210	54	4.5	36
WPSS1025HV	151.2	68	3	52	156	66	2.8	48
WPSS1023HV	164.5	50	4	40	160	46	3.5	35
WPSS1022HV	84	38	3	29	87	35	2.8	27
WPSS1020HV	158.4	59	4	42	168	56	3.6	41
WPSS1018HV	219.6	110	4	59	236	108	3.6	57
WPSS1017HV	172.8	80	4	44	176	74	3.6	40
WPSS1016HV	248.4	82	5	50	250	82	4.6	49
WPSS1015HV	254.4	75	5	47	235	73	5.3	46
WPSS1014HV	243.8	75	5	45	225	73	5.3	42
HRAM1033HV	166.5	61	3	50	150	55	2.6	44
HRAM1034HV	173.6	85	3	54	162	82	3.1	54
WPSS1041HV	220.5	78	5	55	275	67	4.4	51
WPSS1043HV	139.4	45	4	33	132	43	3.9	32
WPSS1044HV	336	108	5	70	350	96	4.8	63
WPSS1045HV	114.7	62	3	36	108	63	3.1	36

ID	R6_profile	R7mean	R7ACL	R7ACPPMe	R7_profile	R8mean	R8ACL	R8ACPPMe
WPSS1002HV	153	64	3.4	45	153	60	3.4	43
WPSS1006HV	135.3	60	2.9	42	121.8	60	2.9	42
ASF1001HV	166.5	75	3.7	46	170.2	77	3.7	46
ASF1002HV	91.2	51	2.4	34	81.6	51	2.4	33
ASF1003HV	125.4	49	3.3	35	115.5	49	3.3	35
ASF1004HV	183.6	79	3.6	49	176.4	79	3.6	50
ASF1005HV	143.5	55	3.5	37	129.5	56	3.5	37
ASF1007HV	86.4	37	3.6	26	93.6	40	3.6	28
ASF1010HV	331.2	148	4.8	82	393.6	121	4.8	73
ASF1013HV	184.8	77	3.3	56	184.8	76	3.3	55
ASF1014HV	108	45	3	33	99	43	3	31
ASF1016HV	118.9	77	2.9	44	127.6	74	2.9	43
ASF1017HV	139.2	70	2.9	48	139.2	71	2.9	48
ASF1019HV	119	50	3.4	36	122.4	53	3.4	37
ASF1021HV	221.4	70	5.4	41	221.4	64	5.4	38
ASF1022HV	126	68	3.6	33	118.8	70	3.6	34
ASF1024HV	280.8	94	3.9	71	276.9	98	3.9	72
ASF1025HV	296.8	74	5.6	52	291.2	77	5.6	53
ASF1026HV	178.6	76	3.8	48	182.4	76	3.8	48
ASF1027HV	80	35	3.2	24	76.8	33	3.2	23
ASF1029HV	89.9	53	3.1	30	93	49	2.9	31
ASF1030HV	173.4	67	3.4	51	173.4	65	3.4	49
ASF1031HV	190	71	3.8	49	186.2	64	3.8	45
ASF1032HV	136.5	62	3.5	46	161	71	3.5	51
ASF1033HV	250.8	95	3.8	58	220.4	108	3.7	64
ASF1037HV	196	70	4	49	196	72	4	50
WPSS1040HV	265.2	97	3.9	66	257.4	94	3.9	64
WPSS1034HV	134.4	45	4.8	28	134.4	45	4.8	28
WPSS1032HV	252	89	4.2	59	247.8	91	4.2	59
WPSS1031HV	155.8	67	3.8	41	155.8	65	3.8	39
WPSS1030HV	196.8	75	4.1	47	192.7	74	4.1	46
WPSS1029HV	408.1	118	5.3	73	386.9	129	5.3	69
WPSS1028HV	176	59	4.4	40	176	57	4.4	39
WPSS1027HV	241.9	101	4.1	60	246	101	4.1	61
WPSS1026HV	162	54	4.5	36	162	50	4.5	34
WPSS1025HV	134.4	69	2.8	49	137.2	67	2.8	47
WPSS1023HV	122.5	47	3.5	32	112	46	3.5	28
WPSS1022HV	75.6	33	2.8	26	72.8	32	2.8	25
WPSS1020HV	147.6	55	3.6	42	151.2	57	3.6	42
WPSS1018HV	205.2	106	3.6	56	201.6	85	3.6	47
WPSS1017HV	144	72	3.6	38	136.8	65	3.6	34
WPSS1016HV	225.4	83	4.6	48	220.8	83	4.6	50
WPSS1015HV	243.8	72	5.3	45	238.5	69	5.3	43
WPSS1014HV	222.6	71	5.3	41	217.3	71	5.3	41
HRAM1033HV	114.4	47	2.6	35	91	47	2.6	35
HRAM1034HV	167.4	84	3.1	54	167.4	83	3.1	50
WPSS1041HV	224.4	65	4.4	48	211.2	64	4.4	46
WPSS1043HV	124.8	41	3.9	30	117	40	3.9	30
WPSS1044HV	302.4	99	4.8	64	307.2	99	4.8	64
WPSS1045HV	111.6	65	3.1	37	114.7	65	3.1	38

ID	R8_profile	R9mean	R9ACL	R9ACPPMe	R9_profile	R10mean	R10ACL	R10ACPPMe
WPSS1002HV	146.2	57	3.4	41	139.4	64	3.4	45
WPSS1006HV	121.8	99999	99999	99999	99999	99999	99999	99999
ASF1001HV	170.2	73	3.7	45	166.5	77	3.7	46
ASF1002HV	79.2	50	2.4	33	79.2	50	2.4	33
ASF1003HV	115.5	50	3.3	35	115.5	53	3.3	38
ASF1004HV	180	77	3.6	48	172.8	74	3.6	48
ASF1005HV	129.5	56	3.5	37	129.5	57	3.5	36
ASF1007HV	100.8	38	3.6	27	97.2	37	3.6	26
ASF1010HV	350.4	142	4.8	78	374.4	140	4.8	79
ASF1013HV	181.5	79	3.3	55	181.5	75	3.3	50
ASF1014HV	93	42	3	29	87	41	3	29
ASF1016HV	124.7	73	2.9	42	121.8	67	2.9	37
ASF1017HV	139.2	71	2.9	46	133.4	70	2.7	46
ASF1019HV	125.8	44	3.4	33	112.2	49	3.4	35
ASF1021HV	205.2	59	5.4	35	189	57	5.4	32
ASF1022HV	122.4	68	3.6	33	118.8	70	3.6	33
ASF1024HV	280.8	78	3.9	53	206.7	97	3.9	67
ASF1025HV	296.8	76	5.6	53	296.8	73	5.6	54
ASF1026HV	182.4	75	3.8	47	178.6	75	3.8	47
ASF1027HV	73.6	32	3.2	22	70.4	32	3.2	22
ASF1029HV	89.9	99999	99999	99999	99999	99999	99999	99999
ASF1030HV	166.6	62	3.4	47	159.8	60	3.4	46
ASF1031HV	171	57	3.8	43	163.4	56	3.8	41
ASF1032HV	178.5	99999	99999	99999	99999	99999	99999	99999
ASF1033HV	236.8	111	3.7	62	229.4	102	3.7	60
ASF1037HV	200	67	4	47	188	68	4	49
WPSS1040HV	249.6	92	3.9	62	241.8	88	3.9	58
WPSS1034HV	134.4	45	4.8	28	134.4	47	4.8	29
WPSS1032HV	247.8	93	4.2	60	252	90	4.2	60
WPSS1031HV	148.2	64	3.8	38	144.4	63	3.8	38
WPSS1030HV	188.6	74	4.1	46	188.6	74	4.1	45
WPSS1029HV	365.7	150	5.3	78	413.4	152	5.3	82
WPSS1028HV	171.6	56	4.4	38	167.2	53	4.4	35
WPSS1027HV	250.1	102	4.1	62	254.2	105	4.1	65
WPSS1026HV	153	51	4.5	35	157.5	51	4.5	35
WPSS1025HV	131.6	60	2.8	43	120.4	60	2.8	42
WPSS1023HV	98	46	3.5	27	94.5	48	3.5	27
WPSS1022HV	70	32	2.8	24	67.2	31	2.8	23
WPSS1020HV	151.2	60	3.6	42	151.2	53	3.6	39
WPSS1018HV	169.2	86	3.6	47	169.2	84	3.6	45
WPSS1017HV	122.4	66	3.6	34	122.4	65	3.6	33
WPSS1016HV	230	81	4.6	48	220.8	79	4.6	47
WPSS1015HV	227.9	68	5.3	43	227.9	67	5.3	43
WPSS1014HV	217.3	73	5.3	43	227.9	73	5.3	43
HRAM1033HV	91	45	2.6	32	83.2	43	2.6	32
HRAM1034HV	155	77	3.1	42	130.2	82	3.1	44
WPSS1041HV	202.4	64	4.4	45	198	64	4.4	44
WPSS1043HV	117	39	3.9	29	113.1	39	3.9	29
WPSS1044HV	307.2	89	4.8	61	292.8	87	4.7	58
WPSS1045HV	117.8	61	2.9	39	113.1	60	2.9	38

ID	R10_profile	S1Sq_Inc_Me	S1SqAUC	S1ACL	S1ACPPMe	S1_profile	S2Sq_Inc_Me
WPSS1002HV	153	192	961	5.4	158	853.2	149
WPSS1006HV	99999	71	360	4.2	60	252	69
ASF1001HV	170.2	146	757	5.9	117	690.3	147
ASF1002HV	79.2	287	1462	5.7	150	855	292
ASF1003HV	125.4	66	331	7.9	61	481.9	62
ASF1004HV	172.8	181	904	7.4	123	910.2	173
ASF1005HV	126	80	418	7.3	56	408.8	103
ASF1007HV	93.6	159	808	7.5	97	727.5	118
ASF1010HV	379.2	163	816	5.4	221	1193.4	172
ASF1013HV	165	96	478	7.5	93	697.5	121
ASF1014HV	87	82	409	4.5	72	324	100
ASF1016HV	107.3	108	540	5.3	90	477	101
ASF1017HV	124.2	172	875	5.4	104	561.6	164
ASF1019HV	119	88	441	6.6	75	495	95
ASF1021HV	172.8	144	721	7.8	94	733.2	120
ASF1022HV	118.8	61	305	7.3	58	423.4	52
ASF1024HV	261.3	23	117	4.3	94	404.2	16
ASF1025HV	302.4	45	226	6	78	468	55
ASF1026HV	178.6	66	332	5.3	78	413.4	51
ASF1027HV	70.4	191	955	6.7	92	616.4	185
ASF1029HV	99999	63	322	4.2	69	289.8	94
ASF1030HV	156.4	35	174	2.5	68	170	38
ASF1031HV	155.8	250	1249	4.9	182	891.8	199
ASF1032HV	99999	224	1121	6.1	127	774.7	170
ASF1033HV	222	132	676	7	141	987	131
ASF1037HV	196	127	381	6.3	116	730.8	21
WPSS1040HV	226.2	34	174	4	98	392	58
WPSS1034HV	139.2	42	213	7.1	52	369.2	34
WPSS1032HV	252	82	420	5.2	91	473.2	77
WPSS1031HV	144.4	209	1044	6.8	131	890.8	182
WPSS1030HV	184.5	42	212	6.6	86	567.6	78
WPSS1029HV	434.6	46	238	5.9	123	725.7	92
WPSS1028HV	154	142	708	5.2	89	462.8	81
WPSS1027HV	266.5	127	649	5.2	130	676	98
WPSS1026HV	157.5	173	883	4.8	115	552	145
WPSS1025HV	117.6	151	738	4.8	117	561.6	128
WPSS1023HV	94.5	247	1237	4.8	169	811.2	239
WPSS1022HV	64.4	173	882	4.9	93	455.7	170
WPSS1020HV	140.4	163	816	5.1	98	499.8	145
WPSS1018HV	162	117	587	4.5	108	486	113
WPSS1017HV	118.8	208	1039	5.5	129	709.5	204
WPSS1016HV	216.2	222	1132	7.4	152	1124.8	210
WPSS1015HV	227.9	52	260	6.6	74	488.4	48
WPSS1014HV	227.9	19	99	5.5	65	357.5	32
HRAM1033HV	83.2	120	852	6	95	570	132
HRAM1034HV	136.4	218	1111	4.7	143	672.1	144
WPSS1041HV	193.6	225	1145	5.1	159	810.9	209
WPSS1043HV	113.1	36	182	5.4	65	351	37
WPSS1044HV	272.6	143	716	5.9	135	796.5	145
WPSS1045HV	110.2	186	948	7.4	131	969.4	326

ID	S2SqAUC	S2ACL	S2ACPPMe	S2_profile	S3Sq_Inc_Me	S3SqAUC	S3ACL
WPSS1002HV	747	5.4	134	723.6	148	754	5.6
WPSS1006HV	343	2.5	68	170	65	325	2.1
ASF1001HV	735	6.8	104	707.2	161	803	7
ASF1002HV	1458	5.3	163	863.9	301	1504	5.6
ASF1003HV	314	8	56	448	58	288	7.9
ASF1004HV	867	7.3	116	846.8	159	813	7.3
ASF1005HV	517	7.2	64	460.8	125	636	7.3
ASF1007HV	600	6.9	89	614.1	123	617	7.2
ASF1010HV	878	5.3	222	1176.6	175	859	5.3
ASF1013HV	628	7.5	100	750	89	446	5.9
ASF1014HV	502	6.5	64	416	110	560	6.4
ASF1016HV	515	5.2	84	436.8	39	196	5.1
ASF1017HV	819	5.5	98	539	159	796	5
ASF1019HV	473	6.6	76	501.6	98	492	6.7
ASF1021HV	601	7.7	91	700.7	126	629	7.9
ASF1022HV	261	6.7	60	402	45	224	6.2
ASF1024HV	78	4.4	104	457.6	27	137	4.4
ASF1025HV	274	6.7	78	522.6	27	135	6
ASF1026HV	260	5.5	66	363	70	352	5.8
ASF1027HV	925	6.7	100	670	183	916	6.7
ASF1029HV	471	4.4	71	312.4	93	463	5.4
ASF1030HV	190	1.7	75	127.5	39	193	4.1
ASF1031HV	993	5.4	169	912.6	216	1082	6
ASF1032HV	850	6	118	708	188	940	5.5
ASF1033HV	654	6.9	143	986.7	242	1233	5.5
ASF1037HV	106	6.4	67	428.8	16	78	6
WPSS1040HV	295	3.7	108	399.6	51	253	3.7
WPSS1034HV	171	7.1	47	333.7	5	23	6.9
WPSS1032HV	393	5	82	410	55	280	4.9
WPSS1031HV	912	6.8	128	870.4	210	1070	6
WPSS1030HV	392	6.1	114	695.4	105	526	7.3
WPSS1029HV	460	5.6	134	750.4	80	399	5.2
WPSS1028HV	403	5.5	91	500.5	103	516	6.8
WPSS1027HV	488	5.1	128	652.8	81	403	5.1
WPSS1026HV	726	5.5	97	533.5	154	770	5.5
WPSS1025HV	652	3.5	131	458.5	109	558	3.3
WPSS1023HV	1197	5.1	159	810.9	239	1197	5.1
WPSS1022HV	852	5	87	435	196	982	5.2
WPSS1020HV	725	4.9	95	465.5	131	655	4.9
WPSS1018HV	564	4.5	101	454.5	99	497	4.5
WPSS1017HV	1040	5.2	132	686.4	204	1043	5.1
WPSS1016HV	1070	6.9	166	1145.4	203	1034	7.3
WPSS1015HV	238	6	71	426	48	242	4.8
WPSS1014HV	161	5.5	67	368.5	41	207	5.2
HRAM1033HV	831	6	103	618	147	941	6
HRAM1034HV	722	4.8	107	513.6	186	949	5.3
WPSS1041HV	1043	5.4	153	826.2	198	1012	5.4
WPSS1043HV	183	4.2	62	260.4	44	231	5.6
WPSS1044HV	737	5.9	136	802.4	148	741	5.9
WPSS1045HV	1628	7.1	153	1086.3	239	1219	6.7

ID	S3ACPPMe	S3_profile	S4Sq_Inc_Me	S4SqAUC	S4ACL	S4ACPPMe	S4_profile
WPSS1002HV	135	756	184	921	5.3	166	879.8
WPSS1006HV	62	130.2	99999	99999	99999	99999	99999
ASF1001HV	108	756	132	701	6.2	114	706.8
ASF1002HV	163	912.8	310	1552	5.2	170	884
ASF1003HV	56	442.4	63	322	7.9	58	458.2
ASF1004HV	107	781.1	134	684	7.3	101	737.3
ASF1005HV	68	496.4	132	648	7.2	65	468
ASF1007HV	87	626.4	98	492	7.1	76	539.6
ASF1010HV	224	1187.2	167	835	5.3	222	1176.6
ASF1013HV	98	578.2	98	492	6.3	96	604.8
ASF1014HV	60	384	93	466	6.7	59	395.3
ASF1016HV	58	295.8	29	146	4.5	63	283.5
ASF1017HV	101	505	165	827	5.2	101	525.2
ASF1019HV	86	576.2	116	582	6.9	91	627.9
ASF1021HV	95	750.5	128	639	8	97	776
ASF1022HV	57	353.4	41	204	6.2	56	347.2
ASF1024HV	105	462	16	82	4.5	95	427.5
ASF1025HV	71	426	35	176	6.5	72	468
ASF1026HV	77	446.6	48	244	5.5	66	363
ASF1027HV	103	690.1	99999	99999	99999	99999	99999
ASF1029HV	59	318.6	69	346	5.8	48	278.4
ASF1030HV	54	221.4	99999	99999	99999	99999	99999
ASF1031HV	157	942	199	993	6.2	143	886.6
ASF1032HV	130	715	185	923	5.5	129	709.5
ASF1033HV	175	962.5	235	1200	5.5	161	885.5
ASF1037HV	69	414	99999	99999	99999	99999	99999
WPSS1040HV	106	392.2	49	243	3.8	98	372.4
WPSS1034HV	42	289.8	24	118	6.9	41	282.9
WPSS1032HV	78	382.2	99999	99999	99999	99999	99999
WPSS1031HV	149	894	215	1098	5.4	157	847.8
WPSS1030HV	125	912.5	110	560	6.8	129	877.2
WPSS1029HV	136	707.2	99999	99999	99999	99999	99999
WPSS1028HV	88	598.4	99999	99999	99999	99999	99999
WPSS1027HV	125	637.5	99999	99999	99999	99999	99999
WPSS1026HV	101	555.5	99999	99999	99999	99999	99999
WPSS1025HV	122	402.6	99999	99999	99999	99999	99999
WPSS1023HV	159	810.9	99999	99999	99999	99999	99999
WPSS1022HV	90	468	187	937	6.8	70	476
WPSS1020HV	91	445.9	99999	99999	99999	99999	99999
WPSS1018HV	87	391.5	99999	99999	99999	99999	99999
WPSS1017HV	130	663	188	942	5.2	128	665.6
WPSS1016HV	156	1138.8	170	866	7.3	140	1022
WPSS1015HV	80	384	99999	99999	99999	99999	99999
WPSS1014HV	74	384.8	41	210	5.6	70	392
HRAM1033HV	111	666	135	675	6.1	112	683.2
HRAM1034HV	121	641.3	162	841	5.2	114	592.8
WPSS1041HV	152	820.8	99999	99999	99999	99999	99999
WPSS1043HV	63	352.8	99999	99999	99999	99999	99999
WPSS1044HV	148	873.2	160	800	5.9	147	867.3
WPSS1045HV	135	904.5	217	1087	6.5	130	845

ID	S5Sq_Inc_Me	S5SqAUC	S5ACL	S5ACPPMe	S5_profile	E_time1	E_time2
WPSS1002HV	165	825	5.4	146	788.4	4.5	1.8
WPSS1006HV	99999	99999	99999	99999	99999	3.8	99999
ASF1001HV	139	805	6.2	114	706.8	6.8	6.1
ASF1002HV	293	1463	5.3	167	885.1	3.7	10.8
ASF1003HV	62	310	7.9	52	410.8	5.2	2.2
ASF1004HV	122	610	7.5	95	712.5	25.5	26.1
ASF1005HV	115	576	7.3	62	452.6	14.1	8.8
ASF1007HV	144	718	7.1	104	738.4	3.3	2.6
ASF1010HV	171	870	5.2	249	1294.8	1.6	1.6
ASF1013HV	85	425	7.6	91	691.6	3.8	3.7
ASF1014HV	105	527	4.6	70	322	4.4	3.5
ASF1016HV	38	192	5.1	57	290.7	2.2	2.1
ASF1017HV	164	819	5.3	97	514.1	5.8	30
ASF1019HV	103	517	6.7	93	623.1	3.8	99999
ASF1021HV	123	616	7.9	95	750.5	5.8	6
ASF1022HV	37	187	6.1	51	311.1	2.1	1.3
ASF1024HV	22	109	4.5	96	432	2.2	2.5
ASF1025HV	42	208	6.2	72	446.4	7	14.1
ASF1026HV	58	291	5.3	71	376.3	4.5	30
ASF1027HV	99999	99999	99999	99999	99999	30	30
ASF1029HV	99999	99999	99999	99999	99999	3.6	2.9
ASF1030HV	99999	99999	99999	99999	99999	8.2	99999
ASF1031HV	179	912	5.6	152	851.2	30	30
ASF1032HV	184	921	5.1	134	683.4	4.9	3.8
ASF1033HV	210	1069	5.6	176	985.6	5.3	3.5
ASF1037HV	99999	99999	99999	99999	99999	2.3	99999
WPSS1040HV	99999	99999	99999	99999	99999	30	30
WPSS1034HV	23	117	6.9	41	282.9	30	30
WPSS1032HV	99999	99999	99999	99999	99999	5.7	99999
WPSS1031HV	216	1081	5.8	148	858.4	21.5	21.5
WPSS1030HV	132	672	7.3	154	1124.2	30	30
WPSS1029HV	99999	99999	99999	99999	99999	30	30
WPSS1028HV	99999	99999	99999	99999	99999	3.4	6.3
WPSS1027HV	99999	99999	99999	99999	99999	18.2	99999
WPSS1026HV	99999	99999	99999	99999	99999	5.3	99999
WPSS1025HV	99999	99999	99999	99999	99999	2.6	99999
WPSS1023HV	99999	99999	99999	99999	99999	30	30
WPSS1022HV	174	871	6	73	438	4.2	4.9
WPSS1020HV	99999	99999	99999	99999	99999	11.3	99999
WPSS1018HV	99999	99999	99999	99999	99999	3.4	99999
WPSS1017HV	202	1009	5.1	130	663	30	30
WPSS1016HV	172	861	7.5	137	1027.5	25.2	28.9
WPSS1015HV	99999	99999	99999	99999	99999	30	99999
WPSS1014HV	44	218	5.6	69	386.4	30	16.8
HRAM1033HV	149	775	6	108	648	14	3
HRAM1034HV	177	901	5.1	113	576.3	8.3	10.9
WPSS1041HV	99999	99999	99999	99999	99999	4.3	6.3
WPSS1043HV	99999	99999	99999	99999	99999	29.6	29.4
WPSS1044HV	99999	99999	99999	99999	99999	18.4	30
WPSS1045HV	99999	99999	99999	99999	99999	23.3	30

ID	E1Sq_Inc_Me	E1SqAUC	E1ACL	E1ACPPMe	E1_profile	E2Sq_Inc_Me	E2SqAUC
WPSS1002HV	113	3441	5.5	109	599.5	113	3441
WPSS1006HV	43	1295	4.4	59	259.6	99999	99999
ASF1001HV	89	2667	5.7	94	535.8	78	2376
ASF1002HV	147	4537	6.1	104	634.4	145	4462
ASF1003HV	44	1252	8	48	384	29	829
ASF1004HV	96	2964	7.4	88	651.2	90	2756
ASF1005HV	72	2184	7.2	51	367.2	60	1833
ASF1007HV	92	2460	6.9	78	538.2	89	2264
ASF1010HV	24	698	5.3	87	461.1	103	3113
ASF1013HV	79	2397	6.3	82	516.6	79	2400
ASF1014HV	60	1858	4.3	48	206.4	41	1236
ASF1016HV	17	535	5.5	43	236.5	17	514
ASF1017HV	109	3295	5.4	83	448.2	127	3839
ASF1019HV	49	1488	6.7	60	402	42	1275
ASF1021HV	88	2705	7.9	80	632	83	2485
ASF1022HV	19	573	5.5	45	247.5	10	316
ASF1024HV	19	583	4.5	94	423	28	844
ASF1025HV	15	458	6.6	64	422.4	20	611
ASF1026HV	46	1373	5.5	70	385	46	1393
ASF1027HV	178	5421	7.1	101	717.1	99	3050
ASF1029HV	27	796	5.5	32	176	32	969
ASF1030HV	12	350	3.8	50	190	99999	99999
ASF1031HV	145	4363	5.4	148	799.2	142	4303
ASF1032HV	111	3342	4.9	100	490	93	2810
ASF1033HV	84	2519	5.4	117	631.8	58	1750
ASF1037HV	19	567	5.5	55	302.5	99999	99999
WPSS1040HV	45	1355	3.8	101	383.8	52	1553
WPSS1034HV	20	612	7.1	40	284	15	466
WPSS1032HV	37	1105	5.1	69	351.9	#NULL!	#NULL!
WPSS1031HV	139	4180	5.9	126	743.4	132	3948
WPSS1030HV	119	3633	8.2	144	1180.8	97	2937
WPSS1029HV	74	2239	5.2	120	624	53	1585
WPSS1028HV	61	1819	5.4	78	421.2	55	1644
WPSS1027HV	56	1691	5	96	480	99999	99999
WPSS1026HV	85	2560	5.9	62	365.8	99999	99999
WPSS1025HV	42	1267	3.3	74	244.2	99999	99999
WPSS1023HV	208	6353	5.7	128	729.6	211	6383
WPSS1022HV	59	1807	4.9	48	235.2	39	1202
WPSS1020HV	78	2367	4.5	75	337.5	99999	99999
WPSS1018HV	47	1429	4.7	57	267.9	99999	99999
WPSS1017HV	145	4395	5.2	105	546	135	4061
WPSS1016HV	115	3453	7.3	113	824.9	131	3989
WPSS1015HV	44	1325	4.9	80	392	99999	99999
WPSS1014HV	17	527	5.2	51	265.2	9	282
HRAM1033HV	98	2972	6	73	438	71	2160
HRAM1034HV	124	3803	5.2	109	566.8	99	3002
WPSS1041HV	116	3552	5.3	114	604.2	77	2342
WPSS1043HV	43	1277	5.4	57	307.8	48	1401
WPSS1044HV	135	4074	6.1	121	738.1	133	4000
WPSS1045HV	143	4309	6.6	97	640.2	143	4331

ID	E2ACL	E2ACPPMe	E2_profile	P1_resid	P1_relax	P2_resid	P2_relax	pre_cough_rest
WPSS1002HV	5.5	109	599.5	69	-5	74	-17	59
WPSS1006HV	99999	99999	99999	54	19	44	30	67
ASF1001HV	5.6	100	560	75	-1	83	-19	69
ASF1002HV	4.7	126	592.2	51	27	32	50	64
ASF1003HV	7.8	42	327.6	60	-24	47	-1	51
ASF1004HV	7.4	84	621.6	57	18	60	23	81
ASF1005HV	6.6	54	356.4	34	20	32	38	49
ASF1007HV	7.3	73	532.9	23	51	30	34	41
ASF1010HV	5.2	108	561.6	138	-4	115	17	135
ASF1013HV	6	88	528	64	20	54	28	76
ASF1014HV	4.8	45	216	13	49	15	68	64
ASF1016HV	5	42	210	76	5	71	15	77
ASF1017HV	4.9	97	475.3	73	-8	49	33	59
ASF1019HV	7.4	40	296	33	19	32	25	48
ASF1021HV	7.8	80	624	67	25	69	17	73
ASF1022HV	6	41	246	49	36	60	24	101
ASF1024HV	4.4	90	396	126	-7	114	-3	120
ASF1025HV	6.7	59	395.3	77	1	69	7	73
ASF1026HV	5.1	69	351.9	75	8	71	12	77
ASF1027HV	7.1	68	482.8	57	-31	46	-4	42
ASF1029HV	5.3	31	164.3	20	63	21	25	31
ASF1030HV	99999	99999	99999	53	-9	46	-36	42
ASF1031HV	5.3	150	795	65	51	67	22	92
ASF1032HV	4.6	96	441.6	46	28	67	9	94
ASF1033HV	5	114	570	57	44	71	37	108
ASF1037HV	99999	99999	99999	59	19	63	8	76
WPSS1040HV	3.8	102	387.6	104	5	93	12	116
WPSS1034HV	6.7	39	261.3	41	6	41	7	43
WPSS1032HV	#NULL!	#NULL!	0	71	12	82	11	80
WPSS1031HV	7.1	105	745.5	58	14	66	-6	64
WPSS1030HV	8.2	127	1041.4	56	-13	68	10	85
WPSS1029HV	3.8	139	528.2	124	13	96	15	125
WPSS1028HV	5.6	71	397.6	53	28	54	24	67
WPSS1027HV	99999	99999	99999	110	2	107	2	104
WPSS1026HV	99999	99999	99999	32	29	39	21	45
WPSS1025HV	99999	99999	99999	57	2	49	3	53
WPSS1023HV	5.4	143	772.2	20	66	26	60	79
WPSS1022HV	5	41	205	28	-17	26	-8	28
WPSS1020HV	99999	99999	99999	66	-2	59	-2	48
WPSS1018HV	99999	99999	99999	74	-20	79	-27	60
WPSS1017HV	5.2	101	525.2	31	56	32	60	62
WPSS1016HV	7.5	115	862.5	49	31	41	48	81
WPSS1015HV	99999	99999	99999	80	0	93	-16	78
WPSS1014HV	5.1	51	260.1	65	-5	64	-7	58
HRAM1033HV	5.9	60	354	29	11	26	13	32
HRAM1034HV	5.1	87	443.7	56	27	44	51	85
WPSS1041HV	5.3	105	556.5	74	-11	63	4	55
WPSS1043HV	5.5	60	330	38	0	41	-14	41
WPSS1044HV	5.9	126	743.4	87	-6	90	9	96
WPSS1045HV	6.7	99	663.3	63	6	71	2	76

ID	C1_cmax	C1r_max	C2_cmax	C2r_max
WPSS1002HV	418	65	402	64
WPSS1006HV	93	68	165	72
ASF1001HV	225	79	232	83
ASF1002HV	232	66	207	69
ASF1003HV	82	52	82	51
ASF1004HV	328	74	316	69
ASF1005HV	81	49	95	53
ASF1007HV	140	50	172	52
ASF1010HV	321	144	369	140
ASF1013HV	143	69	133	83
ASF1014HV	131	66	179	67
ASF1016HV	174	81	138	73
ASF1017HV	197	63	157	62
ASF1019HV	197	61	195	53
ASF1021HV	248	83	179	76
ASF1022HV	212	76	209	79
ASF1024HV	180	137	205	151
ASF1025HV	133	81	134	77
ASF1026HV	113	79	138	83
ASF1027HV	396	50	391	55
ASF1029HV	212	44	175	49
ASF1030HV	99	46	65	35
ASF1031HV	132	91	109	95
ASF1032HV	307	99	297	86
ASF1033HV	247	129	254	118
ASF1037HV	140	74	118	67
WPSS1040HV	202	135	194	98
WPSS1034HV	144	47	109	51
WPSS1032HV	201	96	168	85
WPSS1031HV	280	76	265	75
WPSS1030HV	93	88	104	81
WPSS1029HV	248	135	195	131
WPSS1028HV	226	79	214	71
WPSS1027HV	180	122	216	113
WPSS1026HV	253	88	264	46
WPSS1025HV	278	58	283	58
WPSS1023HV	227	94	223	93
WPSS1022HV	159	26	135	30
WPSS1020HV	163	53	143	60
WPSS1018HV	288	67	322	67
WPSS1017HV	206	75	159	66
WPSS1016HV	132	85	114	82
WPSS1015HV	207	88	193	83
WPSS1014HV	95	63	89	62
HRAM1033HV	102	35	89	38
HRAM1034HV	154	90	198	90
WPSS1041HV	369	68	330	66
WPSS1043HV	116	42	135	44
WPSS1044HV	302	101	282	100
WPSS1045HV	296	85	315	76

Chapter 5 - Traditional measures of normal anorectal function using high-resolution anal manometry in 140 healthy volunteers

ID	sex	age	1	No_preg	No_v_del	N_ins	N_ep	N_tear	anal_rest_mean
002C	0	34	0	0	99999	99999	99999	99999	73
005C	0	46	1	2	0	0	0	0	92
006C	0	31	0	0	99999	99999	99999	99999	66
007B	0	28	0	0	99999	99999	99999	99999	50
007C	0	51	1	3	3	0	2	0	53
008B	0	27	0	0	99999	99999	99999	99999	97
009B	1	25	99999	99999	99999	99999	99999	99999	67
009C	0	43	1	2	1	0	0	0	76
010C	0	45	1	3	3	0	0	1	76
011B	1	32	99999	99999	99999	99999	99999	99999	62
011C	0	47	1	1	1	0	1	0	89
012B	0	28	0	0	99999	99999	99999	99999	94
012C	0	23	0	0	99999	99999	99999	99999	47
013B	1	37	99999	99999	99999	99999	99999	99999	87
013C	0	37	0	0	99999	99999	99999	99999	99
014B	0	55	1	2	2	2	2	0	63
015B	0	50	0	0	99999	99999	99999	99999	111
015C	0	55	1	3	3	2	2	0	101
016B	0	18	0	0	99999	99999	99999	99999	51
017B	0	18	0	0	99999	99999	99999	99999	72
017C	0	37	0	0	99999	99999	99999	99999	56
018B	1	51	99999	99999	99999	99999	99999	99999	71
018C	0	59	1	2	2	0	0	0	33
019B	0	30	0	0	99999	99999	99999	99999	60
019C	0	62	1	2	2	0	0	0	85
020B	0	47	0	0	99999	99999	99999	99999	80
ASF1001HV	0	32	0	0	99999	99999	99999	99999	71
ASF1002HV	0	30	0	0	99999	99999	99999	99999	50
ASF1003HV	0	59	1	2	2	0	1	2	51
ASF1004HV	1	21	99999	99999	99999	99999	99999	99999	72
ASF1005HV	0	33	1	2	0	0	0	0	44
ASF1007HV	1	22	99999	99999	99999	99999	99999	99999	38
ASF1008HV	1	25	99999	99999	99999	99999	99999	99999	114
ASF1010HV	1	49	99999	99999	99999	99999	99999	99999	98
ASF1012HV	1	23	99999	99999	99999	99999	99999	99999	70
ASF1013HV	0	47	1	4	4	0	0	0	78
ASF1014HV	0	35	1	2	1	0	0	1	46
ASF1016HV	0	49	0	0	99999	99999	99999	99999	70
ASF1017HV	0	46	1	1	1	0	0	0	70
ASF1019HV	0	40	1	1	1	0	0	1	48
ASF1021HV	0	44	1	2	2	1	2	1	70
ASF1022HV	0	64	1	3	3	1	1	0	69
ASF1023HV	0	46	1	3	3	0	0	1	76
ASF1024HV	0	49	1	3	3	0	0	1	95
ASF1025HV	0	41	1	1	1	0	0	1	81
ASF1026HV	0	30	1	2	1	0	0	0	76
ASF1027HV	1	63	99999	99999	99999	99999	99999	99999	76
ASF1029HV	1	31	99999	99999	99999	99999	99999	99999	60
ASF1030HV	0	23	0	0	99999	99999	99999	99999	60
ASF1031HV	1	21	99999	99999	99999	99999	99999	99999	65
ASF1032HV	0	33	1	1	1	0	1	0	64

ID	anal_canal_length	sq_mean	sq_max	sq_inc_mean	sq_inc_max	ed_dur	Push_residual
002C	4.8	209	231	126	148	18	87
005C	3.6	311	389	220	299	12	37
006C	5	193	245	130	182	3	40
007B	5	146	178	87	119	10	39
007C	3.7	135	167	90	122	9	43
008B	3.9	208	240	107	139	30	17
009B	5.1	214	319	141	246	3	58
009C	5	305	362	234	291	6	42
010C	4.6	139	182	51	95	5	35
011B	4.5	430	590	366	525	30	41
011C	4.8	176	201	87	112	5	79
012B	5	182	352	97	268	3	33
012C	3.9	199	234	151	186	5	42
013B	3.9	563	732	474	643	21	73
013C	6	387	503	271	387	16	76
014B	3.3	337	375	276	314	9	46
015B	4.3	271	313	156	198	5	58
015C	5.2	209	255	106	152	15	95
016B	2.4	213	238	162	187	26	13
017B	3.7	157	235	99	177	30	26
017C	4	250	296	192	238	7	57
018B	5.3	132	186	64	117	17	48
018C	3.7	147	164	117	134	29	17
019B	4.1	94	168	29	103	2	27
019C	3.6	245	317	153	225	3	76
020B	4.3	180	274	101	195	4	68
ASF1001HV	3.3	218	283	146	212	7	56
ASF1002HV	2.1	331	479	281	429	11	51
ASF1003HV	3.7	117	164	66	113	5	54
ASF1004HV	3.7	238	335	172	268	26	68
ASF1005HV	2.7	158	195	110	147	9	34
ASF1007HV	3.5	184	326	146	287	3	23
ASF1008HV	4.7	184	268	64	147	3	80
ASF1010HV	3.8	223	274	124	176	25	104
ASF1012HV	3.8	126	165	62	101	4	49
ASF1013HV	3.2	177	213	100	135	4	45
ASF1014HV	2.7	148	235	82	169	4	15
ASF1016HV	2.8	172	224	109	160	2	61
ASF1017HV	2.9	240	272	172	204	6	44
ASF1019HV	3.5	153	230	98	175	4	31
ASF1021HV	4.9	199	275	142	218	6	67
ASF1022HV	2.7	128	193	60	125	4	49
ASF1023HV	4	131	263	58	190	2	42
ASF1024HV	3.5	143	170	29	55	3	100
ASF1025HV	3.7	118	132	54	68	14	69
ASF1026HV	3.4	151	199	72	119	29	70
ASF1027HV	3.6	142	199	66	123	30	70
ASF1029HV	2.4	136	168	62	95	4	20
ASF1030HV	3.7	93	103	33	43	8	34
ASF1031HV	2.6	293	354	234	295	30	56
ASF1032HV	3	288	393	218	323	5	43

ID	Push_relax_percent	Push_rectal_peak	RA_grad	anal_c_max	anal_c_inc_max
002C	-2	117	30	186	120
005C	67	88	51	163	62
006C	18	41	1	155	89
007B	25	21	-18	224	181
007C	24	50	7	201	153
008B	83	118	101	210	83
009B	27	88	30	142	66
009C	25	90	48	250	174
010C	56	57	22	151	75
011B	37	93	52	498	434
011C	-1	50	-29	167	89
012B	53	40	7	142	83
012C	45	96	54	239	176
013B	27	140	67	516	413
013C	11	80	4	316	225
014B	28	49	3	138	70
015B	46	200	142	207	98
015C	11	90	-5	166	72
016B	80	50	37	206	157
017B	47	70	44	82	32
017C	5	20	-37	246	178
018B	22	65	17	198	136
018C	10	73	56	143	126
019B	42	18	-9	125	70
019C	14	53	-23	301	207
020B	9	96	28	141	63
ASF1001HV	20	60	4	232	162
ASF1002HV	27	35	-16	232	171
ASF1003HV	-13	21	-33	82	34
ASF1004HV	21	32	-36	346	267
ASF1005HV	21	136	102	95	46
ASF1007HV	51	57	34	140	98
ASF1008HV	29	96	16	278	170
ASF1010HV	2	132	28	218	90
ASF1012HV	40	81	32	122	44
ASF1013HV	45	90	45	133	59
ASF1014HV	68	26	11	179	115
ASF1016HV	25	50	-11	174	97
ASF1017HV	43	58	14	197	139
ASF1019HV	24	23	-8	197	149
ASF1021HV	25	50	-17	248	173
ASF1022HV	36	33	-16	212	140
ASF1023HV	53	80	38	133	35
ASF1024HV	15	76	-24	205	77
ASF1025HV	9	44	-25	134	64
ASF1026HV	14	35	-35	138	61
ASF1027HV	14	74	4	138	62
ASF1029HV	60	35	15	175	143
ASF1030HV	42	120	86	99	57
ASF1031HV	34	45	-11	109	29
ASF1032HV	34	140	97	297	221

ID	sex	age	1	No_preg	No_v_del	N_ins	N_ep	N_tear	anal_rest_mean
ASF1033HV	0	37	0	0	99999	99999	99999	99999	109
ASF1037HV	0	45	1	2	2	0	0	1	72
HRAM1001HV	0	44	1	2	2	1	1	1	53
HRAM1002HV	0	68	1	2	2	0	0	1	62
HRAM1005HV	0	37	1	5	5	1	0	2	67
HRAM1006HV	0	56	1	4	4	0	0	4	40
HRAM1007HV	0	51	1	5	5	3	2	0	72
HRAM1008HV	0	41	1	1	1	0	1	1	47
HRAM1009HV	0	58	1	2	2	1	1	1	64
HRAM1010HV	0	51	1	1	0	0	0	0	64
HRAM1012HV	0	62	1	1	1	0	1	0	71
HRAM1013HV	0	57	1	1	1	0	0	0	107
HRAM1014HV	0	34	1	2	2	1	1	0	54
HRAM1015HV	0	25	1	2	0	0	0	0	50
HRAM1016HV	0	57	1	1	1	0	1	0	85
HRAM1017HV	0	51	1	1	1	0	0	1	60
HRAM1018HV	0	48	1	5	5	0	0	1	55
HRAM1019HV	0	56	1	1	0	0	0	0	69
HRAM1020HV	0	31	1	1	1	0	0	0	33
HRAM1021HV	0	40	1	2	1	1	1	0	59
HRAM1022HV	0	62	1	2	2	1	1	0	62
HRAM1023HV	0	57	1	2	2	0	0	2	29
HRAM1024HV	0	46	1	4	4	0	0	0	52
HRAM1025HV	0	44	1	3	3	0	0	0	33
HRAM1026HV	0	53	1	2	2	0	0	0	35
HRAM1027HV	0	49	1	1	0	0	0	0	25
HRAM1028HV	0	37	1	3	2	1	1	0	59
HRAM1029HV	0	54	1	4	4	1	0	0	54
HRAM1031HV	0	31	1	1	0	0	0	0	48
HRAM1033HV	0	41	0	0	99999	99999	99999	99999	54
HRAM1034HV	0	25	0	0	99999	99999	99999	99999	83
HRAM1035HV	0	21	0	0	99999	99999	99999	99999	58
HRAM1036HV	0	35	0	0	99999	99999	99999	99999	63
HRAM1037HV	1	57	99999	99999	99999	99999	99999	99999	53
HRAM1038HV	0	59	0	0	99999	99999	99999	99999	50
HRAM1039HV	0	35	1	3	3	0	0	0	75
HRAM1040HV	0	50	0	0	99999	99999	99999	99999	50
HRAM1041HV	0	30	0	0	99999	99999	99999	99999	65
HRAM1042HV	0	33	0	0	99999	99999	99999	99999	56
HRAM1043HV	0	39	0	0	99999	99999	99999	99999	44
HRAM1044HV	1	65	99999	99999	99999	99999	99999	99999	83
HRAM1047HV	1	64	99999	99999	99999	99999	99999	99999	54
HRAM1048HV	1	35	99999	99999	99999	99999	99999	99999	74
HRAM1049HV	1	35	99999	99999	99999	99999	99999	99999	88
HRAM1050HV	1	48	99999	99999	99999	99999	99999	99999	118
HRAM1051HV	0	22	0	0	99999	99999	99999	99999	54
HRAM1054HV	1	59	99999	99999	99999	99999	99999	99999	86
HRAM1055HV	1	60	99999	99999	99999	99999	99999	99999	48
HRAM1056HV	0	27	1	1	1	0	0	1	61
HRAM1057HV	0	27	0	0	99999	99999	99999	99999	53
HRAM1058HV	1	27	99999	99999	99999	99999	99999	99999	77

ID	anal_canal_length	sq_mean	sq_max	sq_inc_mean	sq_inc_max	ed_dur	Push_residual
ASF1033HV	3.7	335	428	234	327	5	71
ASF1037HV	3.6	158	260	95	196	2	60
HRAM1001HV	2.9	131	166	77	112	30	50
HRAM1002HV	4.2	93	111	29	48	8	40
HRAM1005HV	3.5	139	238	80	178	9	65
HRAM1006HV	3.3	169	196	130	157	16	33
HRAM1007HV	4.4	112	133	90	111	5	29
HRAM1008HV	3.8	83	113	42	72	30	24
HRAM1009HV	2.5	80	100	23	43	3	46
HRAM1010HV	2.3	174	246	104	175	3	29
HRAM1012HV	3.1	105	122	43	60	6	39
HRAM1013HV	3.2	151	164	44	57	19	61
HRAM1014HV	3.9	186	236	133	184	6	52
HRAM1015HV	3.2	70	103	35	68	4	26
HRAM1016HV	3.6	99	123	56	80	3	31
HRAM1017HV	2.6	107	146	55	94	30	38
HRAM1018HV	4.5	170	215	132	176	5	43
HRAM1019HV	3.4	197	258	162	224	8	16
HRAM1020HV	2.3	56	76	36	57	4	15
HRAM1021HV	2.6	136	188	110	162	6	22
HRAM1022HV	2.9	151	210	98	157	6	40
HRAM1023HV	1.6	157	191	135	170	20	19
HRAM1024HV	2.4	109	138	61	90	4	29
HRAM1025HV	3.4	187	225	157	195	5	29
HRAM1026HV	2.9	24	180	93	149	3	32
HRAM1027HV	2.9	132	187	110	165	6	12
HRAM1028HV	3	156	202	85	131	29	46
HRAM1029HV	3.8	75	82	21	28	16	56
HRAM1031HV	2.5	178	215	124	162	10	55
HRAM1033HV	2.4	182	240	131	189	14	26
HRAM1034HV	2.5	293	421	212	340	17	44
HRAM1035HV	3.3	187	242	130	184	3	55
HRAM1036HV	3	199	267	116	184	3	35
HRAM1037HV	2.9	190	212	136	158	30	43
HRAM1038HV	3.2	148	203	102	157	11	54
HRAM1039HV	3.6	248	302	168	223	5	76
HRAM1040HV	3.2	255	332	212	289	8	33
HRAM1041HV	4.1	290	332	229	272	4	31
HRAM1042HV	4.5	109	133	59	83	28	51
HRAM1043HV	2.8	263	346	216	299	7	34
HRAM1044HV	4.5	212	360	126	275	3	97
HRAM1047HV	4.5	133	165	70	102	30	101
HRAM1048HV	5.8	378	571	293	487	3	77
HRAM1049HV	4.7	432	490	337	396	29	61
HRAM1050HV	4.7	261	351	150	235	25	76
HRAM1051HV	2	84	92	37	45	30	24
HRAM1054HV	6	329	415	235	322	30	105
HRAM1055HV	3.1	168	267	115	214	3	64
HRAM1056HV	3.4	173	263	116	205	4	21
HRAM1057HV	4.1	108	124	54	70	5	56
HRAM1058HV	4.8	216	409	135	328	1	74

ID	Push_relax_percent	Push_rectal_peak	RA_grad	anal_c_max	anal_c_inc_max
ASF1033HV	37	90	19	254	147
ASF1037HV	12	100	40	140	73
HRAM1001HV	61	87	37	101	42
HRAM1002HV	28	134	94	160	107
HRAM1005HV	-17	94	29	209	170
HRAM1006HV	12	77	44	138	103
HRAM1007HV	17	55	26	226	155
HRAM1008HV	32	40	16	165	129
HRAM1009HV	15	70	24	66	17
HRAM1010HV	64	66	37	209	132
HRAM1012HV	40	76	37	115	53
HRAM1013HV	47	95	34	171	51
HRAM1014HV	4	32	-20	154	102
HRAM1015HV	24	50	24	253	202
HRAM1016HV	3	65	34	118	83
HRAM1017HV	38	85	47	104	55
HRAM1018HV	33	89	46	101	38
HRAM1019HV	50	67	51	243	174
HRAM1020HV	22	22	7	58	37
HRAM1021HV	28	57	35	80	56
HRAM1022HV	22	35	-5	205	154
HRAM1023HV	38	60	41	184	151
HRAM1024HV	32	36	7	112	74
HRAM1025HV	6	100	71	112	79
HRAM1026HV	-6	76	44	68	45
HRAM1027HV	45	38	26	158	141
HRAM1028HV	30	51	5	146	78
HRAM1029HV	-14	37	-19	90	42
HRAM1031HV	17	90	35	460	408
HRAM1033HV	13	44	18	105	72
HRAM1034HV	51	61	17	154	74
HRAM1035HV	6	52	-3	174	115
HRAM1036HV	29	55	20	160	109
HRAM1037HV	14	53	10	379	326
HRAM1038HV	7	57	3	120	64
HRAM1039HV	-12	28	-48	204	141
HRAM1040HV	-11	39	6	230	203
HRAM1041HV	46	31	0	271	216
HRAM1042HV	15	29	-22	121	57
HRAM1043HV	37	48	14	240	194
HRAM1044HV	-4	69	-28	169	83
HRAM1047HV	-26	108	7	140	84
HRAM1048HV	2	160	83	485	403
HRAM1049HV	35	60	-1	317	212
HRAM1050HV	38	209	133	344	228
HRAM1051HV	47	30	6	91	50
HRAM1054HV	-4	134	29	328	224
HRAM1055HV	-12	72	8	276	215
HRAM1056HV	65	34	13	115	47
HRAM1057HV	-1	33	-23	100	48
HRAM1058HV	13	80	6	301	215

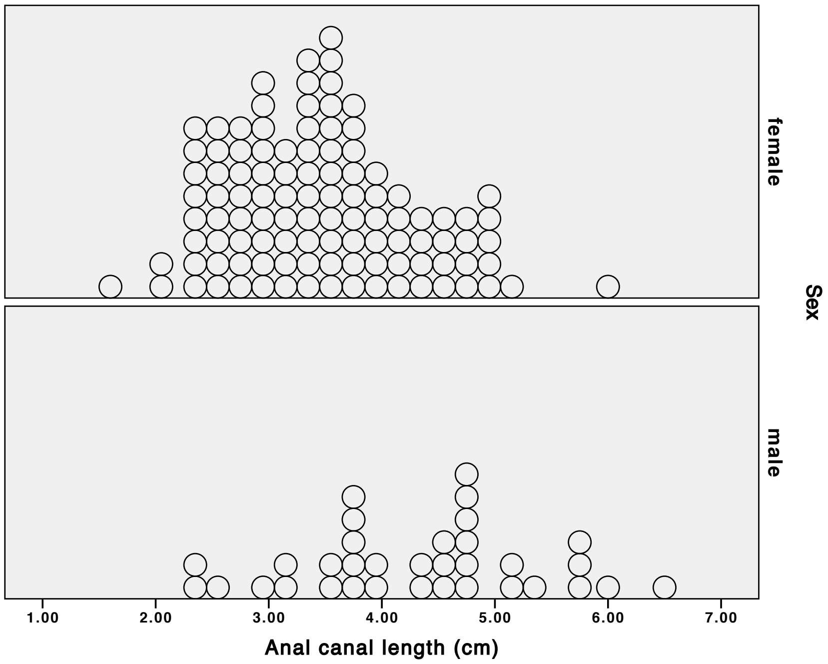
ID	sex	age	1	No_preg	No_v_del	N_ins	N_ep	N_tear	anal_rest_mean
HRAM1059HV	0	24	0	0	99999	99999	99999	99999	85
HRAM1060HV	1	32	99999	99999	99999	99999	99999	99999	84
HRAM1061HV	1	46	99999	99999	99999	99999	99999	99999	76
HRAM1062HV	1	50	99999	99999	99999	99999	99999	99999	103
HRAM1063HV	1	42	99999	99999	99999	99999	99999	99999	72
HRAM1066HV	1	57	99999	99999	99999	99999	99999	99999	79
HRAM1067HV	0	54	0	0	99999	99999	99999	99999	56
HRAM1068HV	1	37	99999	99999	99999	99999	99999	99999	65
HRAM1069HV	0	33	0	0	99999	99999	99999	99999	52
WPSS1002HV	1	36	99999	99999	99999	99999	99999	99999	60
WPSS1006HV	1	47	99999	99999	99999	99999	99999	99999	61
WPSS1007HV	0	30	1	1	1	0	0	0	55
WPSS1009HV	0	58	0	0	99999	99999	99999	99999	63
WPSS1010HV	0	59	1	1	1	0	0	0	35
WPSS1011HV	0	45	1	1	1	0	0	0	59
WPSS1013HV	1	72	99999	99999	99999	99999	99999	99999	58
WPSS1014HV	0	53	1	1	3	1	0	0	73
WPSS1015HV	0	31	0	0	99999	99999	99999	99999	70
WPSS1016HV	0	36	0	0	99999	99999	99999	99999	81
WPSS1017HV	0	23	0	0	99999	99999	99999	99999	65
WPSS1018HV	0	65	0	0	99999	99999	99999	99999	83
WPSS1020HV	0	68	0	0	99999	99999	99999	99999	56
WPSS1022HV	0	35	1	1	1	1	1	1	31
WPSS1023HV	0	57	0	0	99999	99999	99999	99999	46
WPSS1025HV	0	57	1	2	0	0	0	0	63
WPSS1026HV	0	36	1	1	1	0	0	1	49
WPSS1027HV	0	31	1	2	1	0	1	1	102
WPSS1028HV	0	23	0	0	99999	99999	99999	99999	56
WPSS1029HV	1	21	99999	99999	99999	99999	99999	99999	136
WPSS1030HV	0	63	1	2	2	0	2	0	74
WPSS1031HV	0	25	0	0	99999	99999	99999	99999	66
WPSS1032HV	0	46	1	2	2	0	0	1	91
WPSS1034HV	1	47	99999	99999	99999	99999	99999	99999	47
WPSS1040HV	0	50	1	3	3	0	0	1	91
WPSS1041HV	1	33	99999	99999	99999	99999	99999	99999	64
WPSS1043HV	0	51	1	2	2	0	1	1	39
WPSS1044HV	1	25	99999	99999	99999	99999	99999	99999	89
WPSS1045HV	0	44	0	0	99999	99999	99999	99999	61

ID	anal_canal_length	sq_mean	sq_max	sq_inc_mean	sq_inc_max	ed_dur	Push_residual
HRAM1059HV	3.4	257	323	182	248	9	62
HRAM1060HV	5.7	323	476	239	391	2	72
HRAM1061HV	4.4	184	278	120	215	2	51
HRAM1062HV	3.9	330	487	227	384	20	67
HRAM1063HV	6.5	228	276	149	197	18	68
HRAM1066HV	4.8	188	226	140	178	30	46
HRAM1067HV	2.7	260	335	204	278	2	38
HRAM1068HV	5.8	170	252	90	172	4	69
HRAM1069HV	2.4	164	261	80	147	21	41
WPSS1002HV	3.2	127	246	111	230	28	57
WPSS1006HV	2.3	120	179	50	110	5	44
WPSS1007HV	2.7	133	170	71	108	10	40
WPSS1009HV	3.5	63	81	37	55	3	19
WPSS1010HV	2.5	96	118	73	95	5	31
WPSS1011HV	3.2	94	117	72	94	5	24
WPSS1013HV	3.7	86	94	54	62	23	26
WPSS1014HV	4.3	96	102	20	27	30	62
WPSS1015HV	4.7	77	91	53	66	30	23
WPSS1016HV	4.7	299	338	222	260	25	42
WPSS1017HV	2.6	266	289	210	233	30	31
WPSS1018HV	2.4	210	267	117	175	3	62
WPSS1020HV	3	220	318	163	261	5	59
WPSS1022HV	2.6	201	260	174	232	4	29
WPSS1023HV	3	294	319	239	265	30	26
WPSS1025HV	2.8	195	377	127	309	3	53
WPSS1026HV	4.1	198	280	148	231	5	32
WPSS1027HV	3.6	226	249	127	150	18	110
WPSS1028HV	3.5	190	239	139	188	3	70
WPSS1029HV	5.1	198	274	49	125	4	93
WPSS1030HV	4.5	165	184	105	124	30	46
WPSS1031HV	3.4	276	298	211	233	22	58
WPSS1032HV	4	173	218	85	130	6	71
WPSS1034HV	3.7	92	113	40	61	5	41
WPSS1040HV	3.3	146	182	57	94	10	109
WPSS1041HV	4.3	293	397	230	334	5	60
WPSS1043HV	3.5	74	83	36	45	30	36
WPSS1044HV	4.7	230	260	146	176	19	79
WPSS1045HV	2.3	245	273	183	211	23	68

ID	Push_relax_percent	Push_rectal_peak	RA_grad	anal_c_max	anal_c_inc_max
HRAM1059HV	16	45	-17	174	103
HRAM1060HV	15	48	-24	150	65
HRAM1061HV	24	13	-38	75	16
HRAM1062HV	37	116	49	173	68
HRAM1063HV	11	24	-44	107	32
HRAM1066HV	-12	47	1	215	172
HRAM1067HV	31	104	66	313	253
HRAM1068HV	-12	95	26	268	212
HRAM1069HV	6	60	19	146	107
WPSS1002HV	-100	85	28	299	270
WPSS1006HV	30	47	3	165	98
WPSS1007HV	27	52	12	113	65
WPSS1009HV	7	50	31	118	96
WPSS1010HV	-16	48	17	112	90
WPSS1011HV	3	49	25	216	194
WPSS1013HV	-4	20	-6	158	128
WPSS1014HV	-3	37	-25	95	36
WPSS1015HV	-1	20	-3	160	136
WPSS1016HV	47	75	33	114	34
WPSS1017HV	56	21	-10	159	94
WPSS1018HV	4	38	-24	288	224
WPSS1020HV	-1	68	9	188	137
WPSS1022HV	-3	40	11	137	108
WPSS1023HV	66	74	48	227	149
WPSS1025HV	7	57	4	278	227
WPSS1026HV	29	49	17	264	219
WPSS1027HV	3	22	-88	216	112
WPSS1028HV	5	118	48	226	153
WPSS1029HV	12	77	-16	248	123
WPSS1030HV	10	50	4	93	7
WPSS1031HV	15	54	-4	280	214
WPSS1032HV	12	40	-31	201	121
WPSS1034HV	6	22	-19	144	101
WPSS1040HV	6	73	-36	194	108
WPSS1041HV	9	79	19	369	307
WPSS1043HV	5	59	23	112	75
WPSS1044HV	8	80	1	282	191
WPSS1045HV	0	68	0	315	243

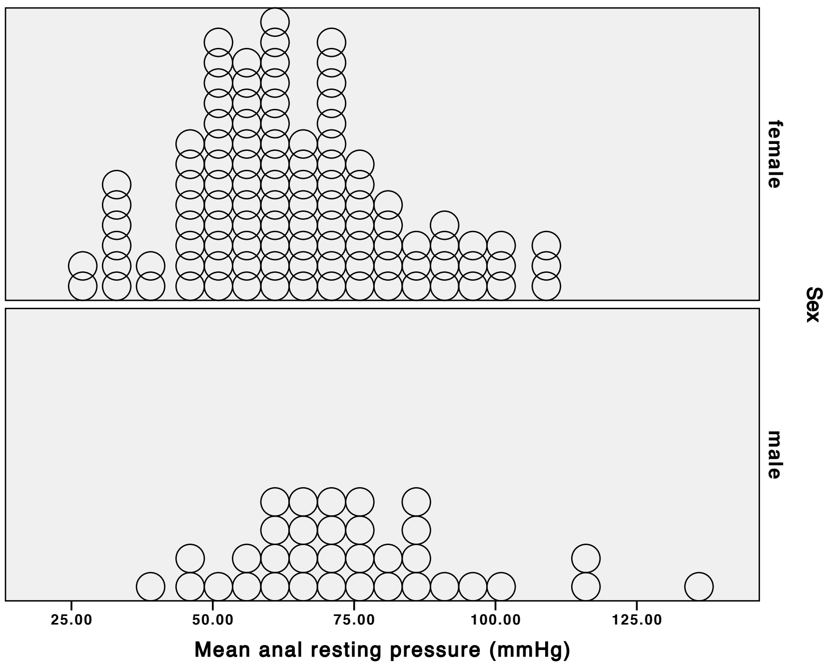
REST (1)

Anal canal length – by sex



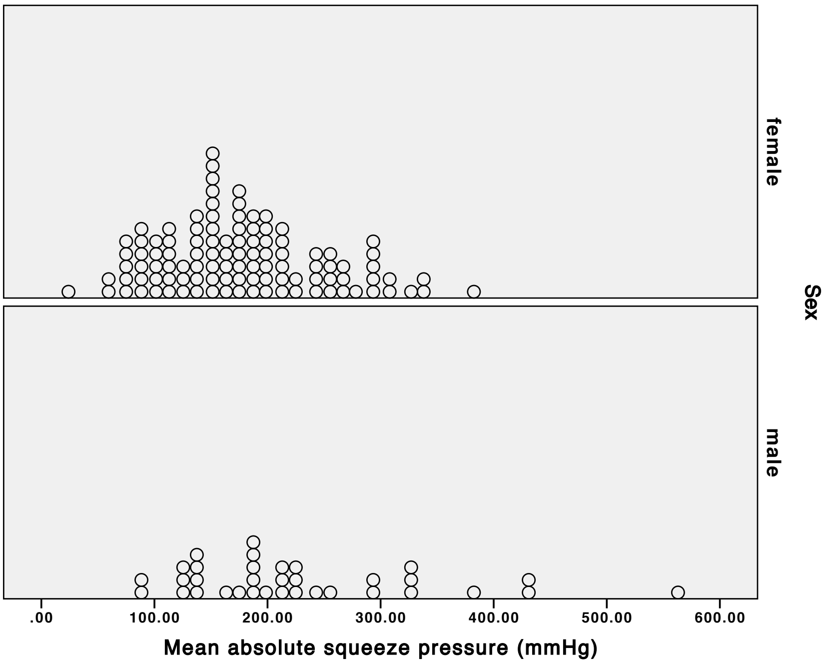
REST (2)

Mean anal canal resting pressure – by sex

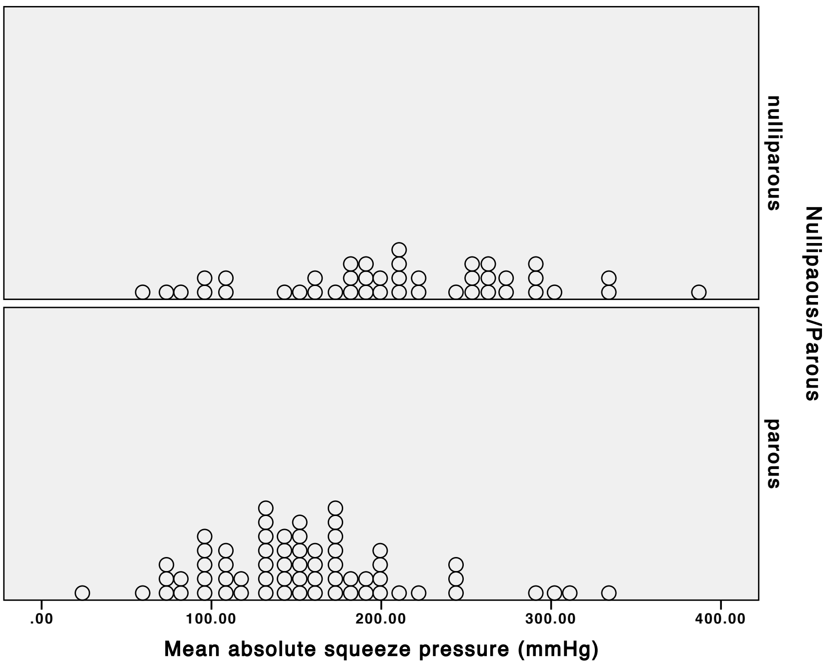


SQUEEZE (1)

Mean absolute squeeze pressure – by sex

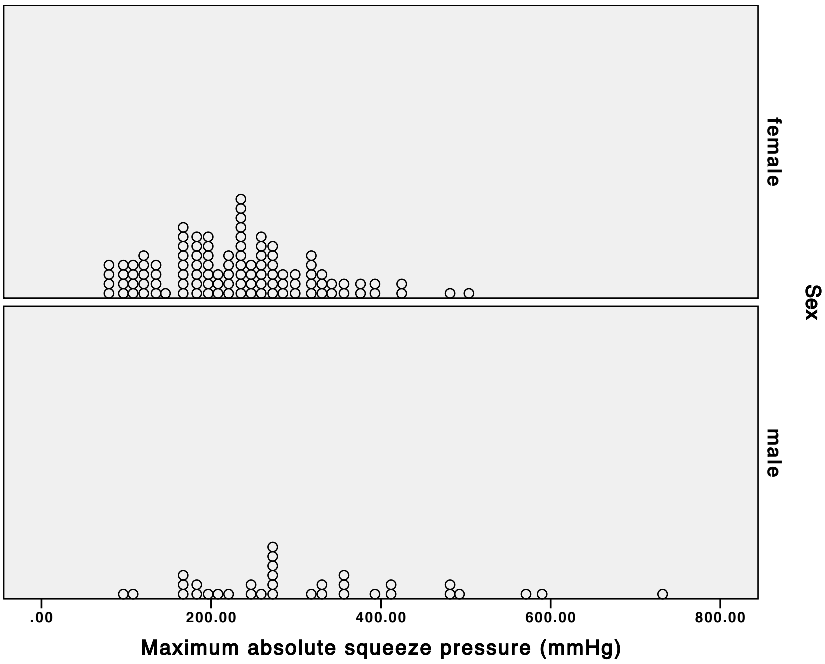


Mean absolute squeeze pressure in females – by parity

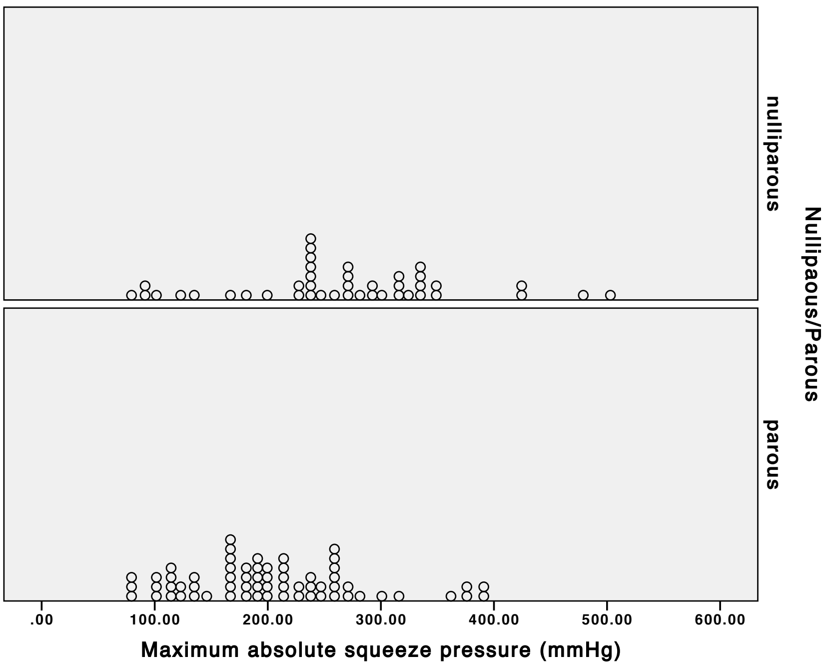


SQUEEZE (2)

Maximum absolute squeeze pressure – by sex

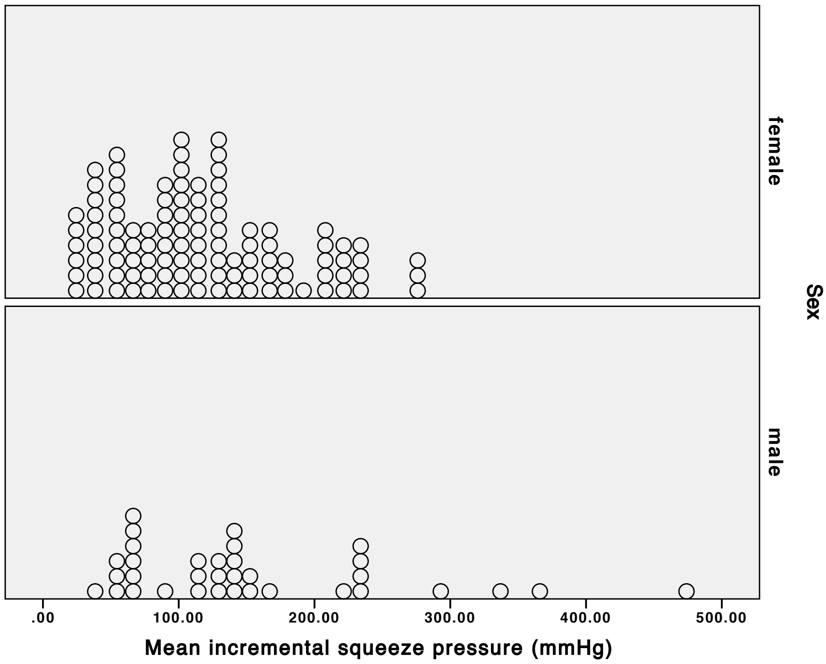


Maximum absolute squeeze pressure – in females by parity

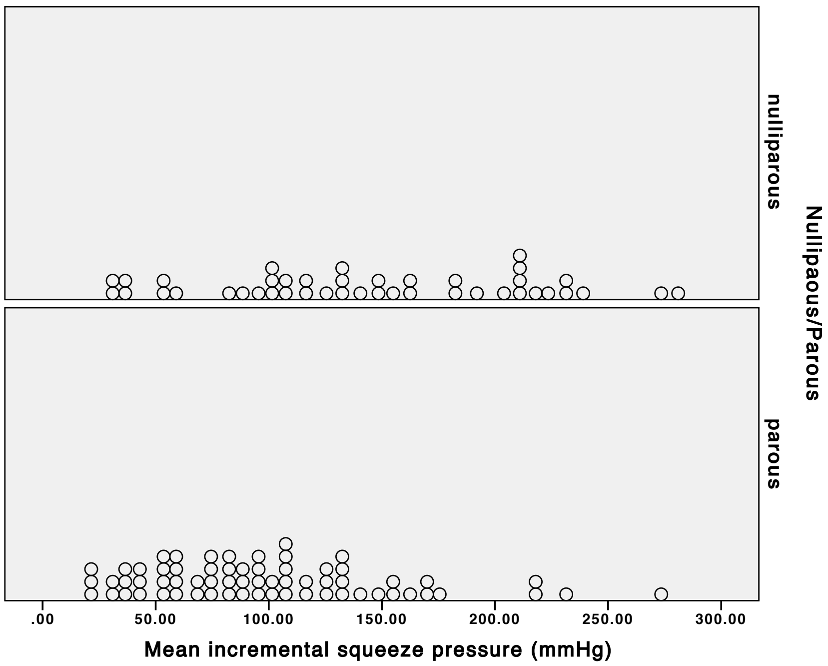


SQUEEZE (3)

Mean incremental squeeze pressure – by sex

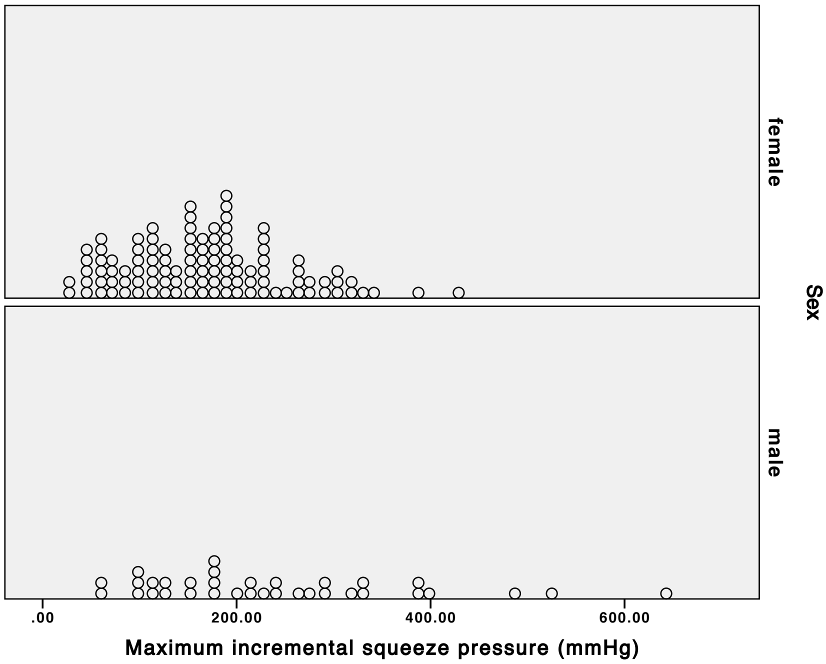


Mean incremental squeeze pressure – in females by parity

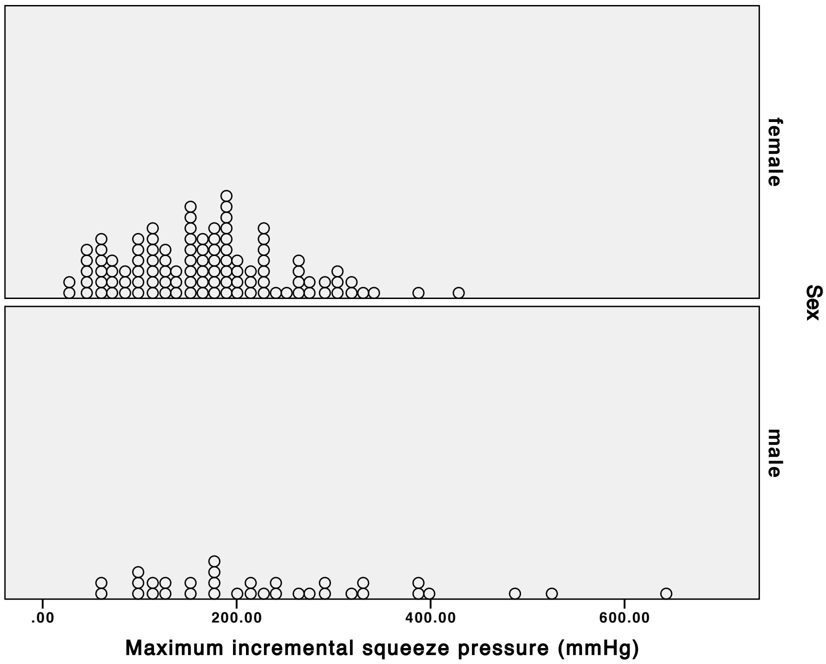


SQUEEZE (4)

Maximum incremental squeeze pressure – by sex

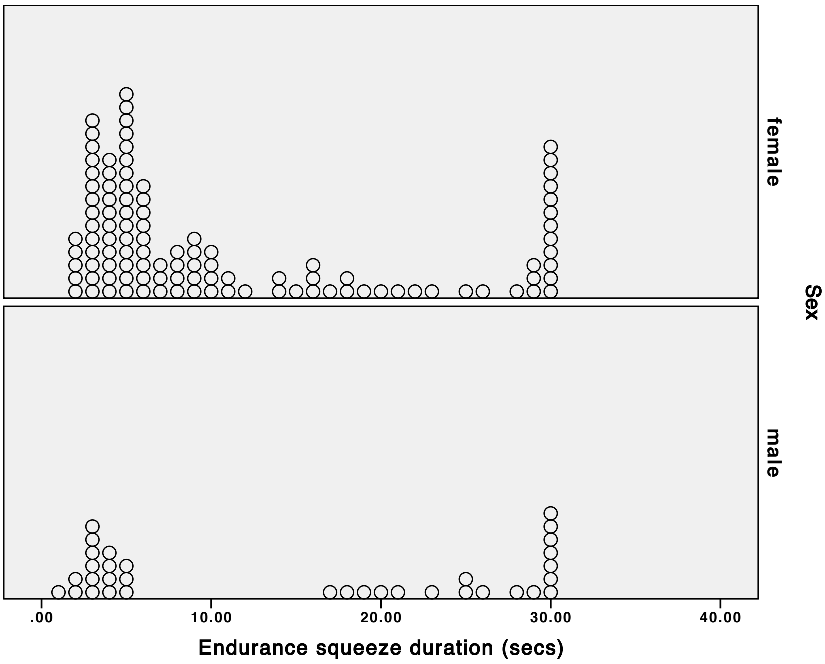


Maximum incremental squeeze pressure – in females by parity



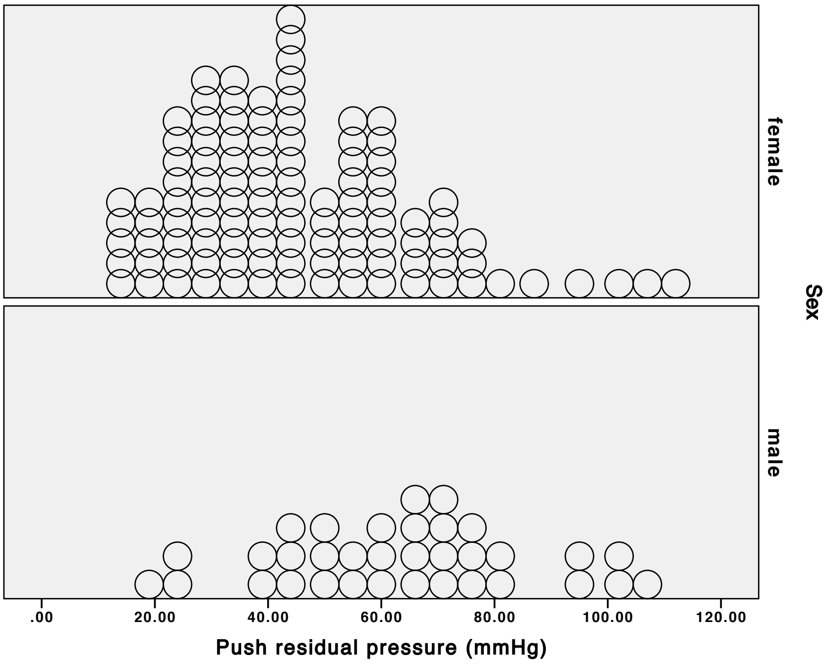
ENDURANCE SQUEEZE (1)

Endurance squeeze duration – by sex



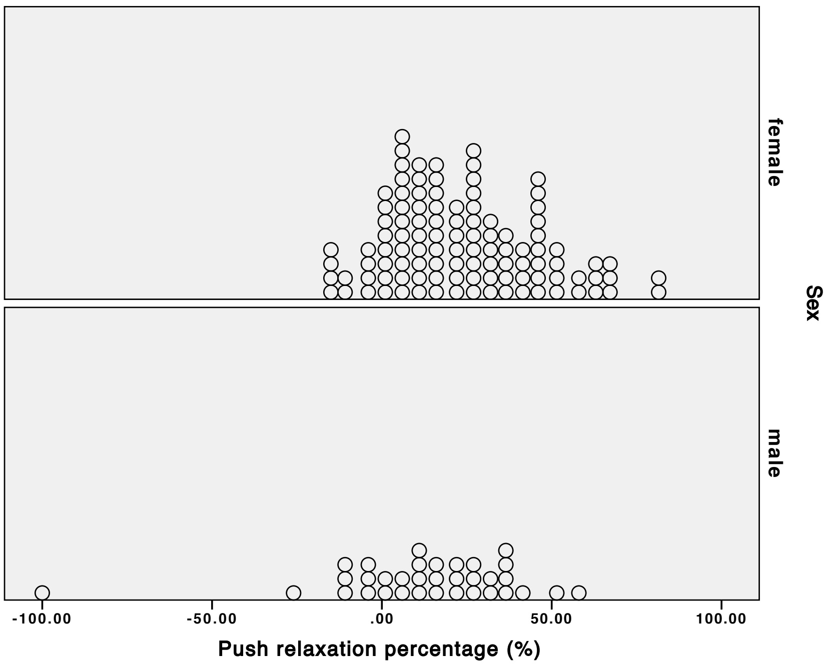
PUSH (1)

Push residual pressure – by sex



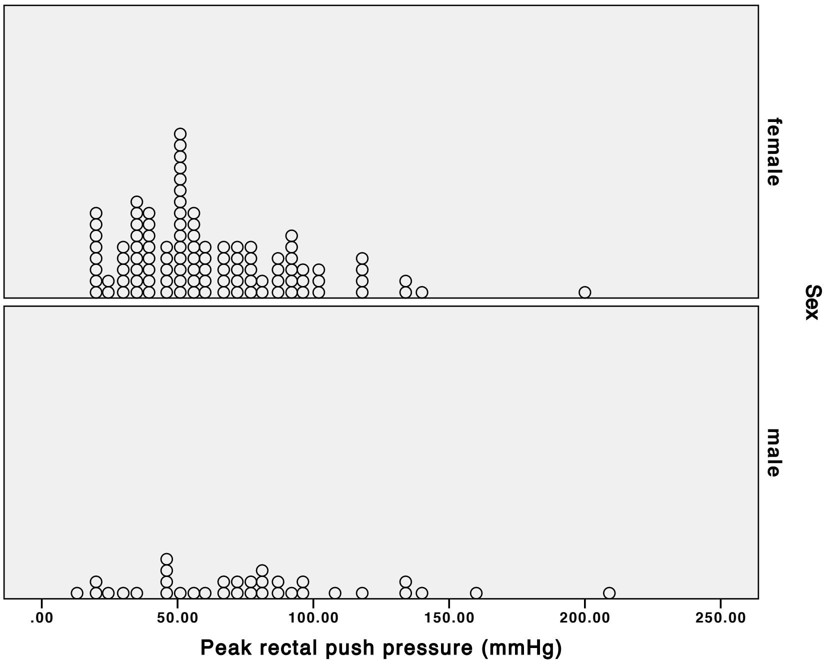
PUSH (2)

Push relaxation percentage – by sex



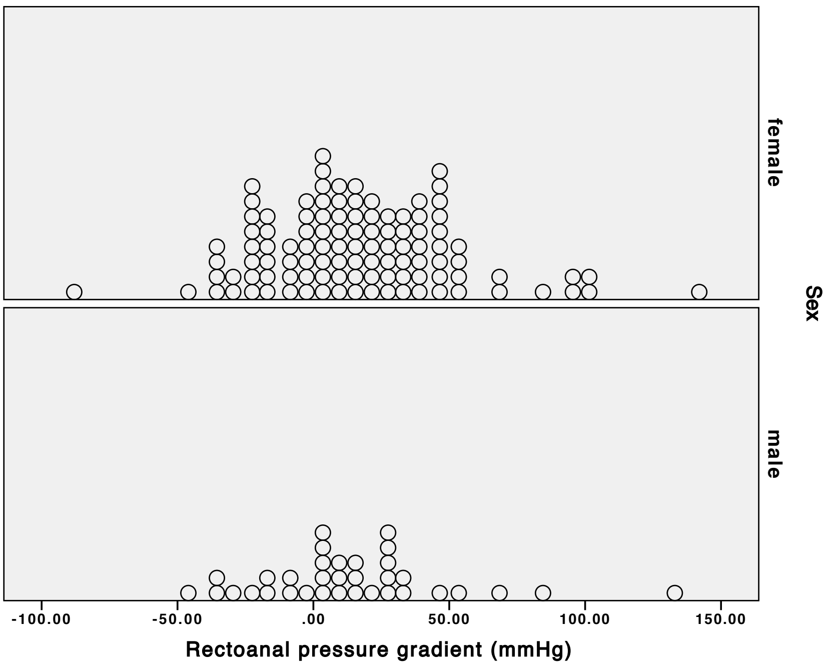
PUSH (3)

Peak rectal push pressure – by sex



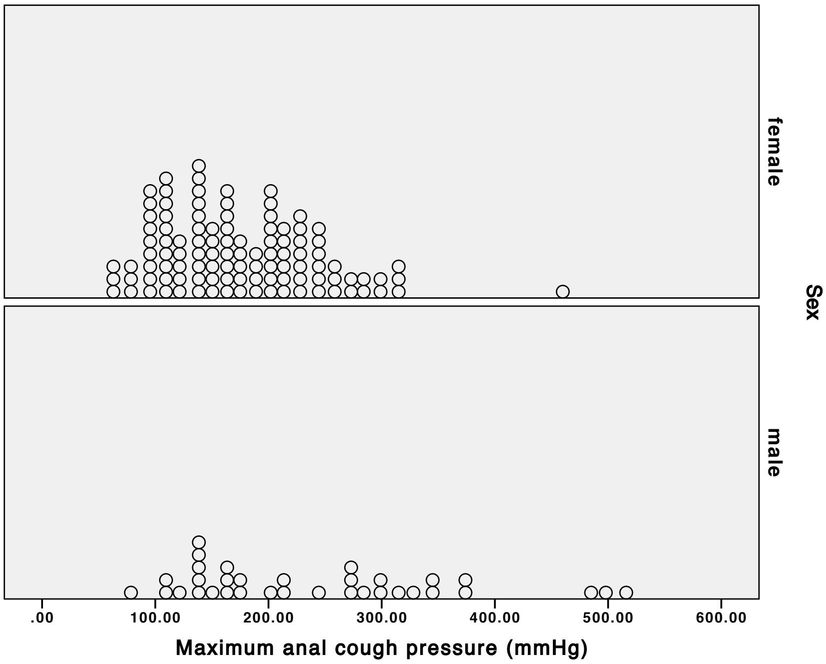
PUSH (4)

Rectoanal pressure gradient – by sex



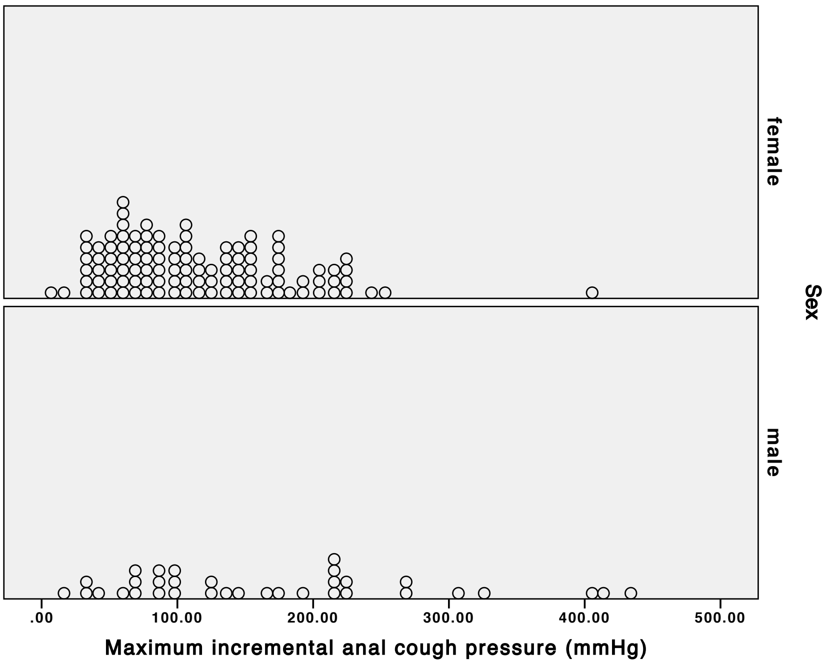
COUGH (1)

Maximum anal cough pressure



COUGH (2)

Maximum incremental anal cough pressure – by sex



Chapter 6 - Anal sphincter profiles: development and analysis of a novel instrument for assessment of anal motor function using high resolution anorectal manometry

ID	Group	Sex	Age	Children	Symptoms	Urge_symptoms	External_muscle
WPSS1006HV	0	0	23	0	99999	99999	99999
ASF1001HV	0	0	33	0	99999	99999	99999
ASF1002HV	0	0	54	1	99999	99999	99999
ASF1003HV	0	0	31	0	99999	99999	99999
ASF1005HV	0	0	35	1	99999	99999	99999
ASF1013HV	0	0	47	1	99999	99999	99999
ASF1014HV	0	0	35	1	99999	99999	99999
ASF1016HV	0	0	48	0	99999	99999	99999
ASF1017HV	0	0	46	1	99999	99999	99999
ASF1019HV	0	0	40	1	99999	99999	99999
ASF1021HV	0	0	44	1	99999	99999	99999
ASF1023HV	0	0	45	1	99999	99999	99999
ASF1024HV	0	0	49	1	99999	99999	99999
ASF1025HV	0	0	41	1	99999	99999	99999
ASF1026HV	0	0	30	1	99999	99999	99999
ASF1030HV	0	0	22	0	99999	99999	99999
ASF1032HV	0	0	33	1	99999	99999	99999
ASF1033HV	0	0	37	0	99999	99999	99999
ASF1037HV	0	0	45	1	99999	99999	99999
WPSS1040HV	0	0	50	1	99999	99999	99999
WPSS1032HV	0	0	45	1	99999	99999	99999
WPSS1031HV	0	0	25	0	99999	99999	99999
WPSS1028HV	0	0	23	0	99999	99999	99999
WPSS1027HV	0	0	31	1	99999	99999	99999
WPSS1026HV	0	0	35	1	99999	99999	99999
WPSS1025HV	0	0	57	1	99999	99999	99999
WPSS1023HV	0	0	57	0	99999	99999	99999
WPSS1022HV	0	0	35	1	99999	99999	99999
WPSS1020HV	0	0	68	0	99999	99999	99999
WPSS1018HV	0	0	65	0	99999	99999	99999
WPSS1017HV	0	0	23	0	99999	99999	99999
WPSS1016HV	0	0	36	0	99999	99999	99999
WPSS1015HV	0	0	61	0	99999	99999	99999
WPSS1014HV	0	0	53	1	99999	99999	99999
WPSS1043HV	0	0	51	1	99999	99999	99999
WPSS1045HV	0	0	44	0	99999	99999	99999
HRAM1001HV	0	0	44	1	99999	99999	99999
HRAM1002HV	0	0	68	1	99999	99999	99999
HRAM1005HV	0	0	37	1	99999	99999	99999
HRAM1006HV	0	0	56	1	99999	99999	99999
HRAM1007HV	0	0	51	1	99999	99999	99999
HRAM1008HV	0	0	41	1	99999	99999	99999
HRAM1009HV	0	0	58	1	99999	99999	99999
HRAM1010HV	0	0	51	1	99999	99999	99999
HRAM1013HV	0	0	57	1	99999	99999	99999
HRAM1014HV	0	0	34	1	99999	99999	99999
HRAM1015HV	0	0	25	1	99999	99999	99999
HRAM1016HV	0	0	57	1	99999	99999	99999
HRAM1017HV	0	0	51	1	99999	99999	99999

ID	Internal_muscle	Vaizey_score	conventional_Sq	normal_convent	new_squeeze
WPSS1006HV	99999	1	56	0	71
ASF1001HV	99999	0	90	0	146
ASF1002HV	99999	0	88	0	287
ASF1003HV	99999	0	58	0	66
ASF1005HV	99999	0	99999	99999	80
ASF1013HV	99999	2	99999	99999	96
ASF1014HV	99999	0	90	0	82
ASF1016HV	99999	1	56	0	108
ASF1017HV	99999	2	99999	99999	172
ASF1019HV	99999	0	99999	99999	88
ASF1021HV	99999	0	99999	99999	144
ASF1023HV	99999	1	99999	99999	58
ASF1024HV	99999	1	99999	99999	23
ASF1025HV	99999	2	99999	99999	45
ASF1026HV	99999	0	82	0	66
ASF1030HV	99999	3	99999	99999	35
ASF1032HV	99999	2	99999	99999	224
ASF1033HV	99999	2	99999	99999	132
ASF1037HV	99999	2	99999	99999	127
WPSS1040HV	99999	1	99999	99999	34
WPSS1032HV	99999	1	44	0	82
WPSS1031HV	99999	0	102	0	209
WPSS1028HV	99999	0	60	0	142
WPSS1027HV	99999	0	78	0	127
WPSS1026HV	99999	0	104	0	173
WPSS1025HV	99999	1	53	0	151
WPSS1023HV	99999	0	38	0	247
WPSS1022HV	99999	1	99999	99999	173
WPSS1020HV	99999	0	91	0	163
WPSS1018HV	99999	1	37	0	117
WPSS1017HV	99999	0	99999	99999	208
WPSS1016HV	99999	2	99999	99999	222
WPSS1015HV	99999	2	40	0	52
WPSS1014HV	99999	0	99999	99999	19
WPSS1043HV	99999	1	40	0	36
WPSS1045HV	99999	0	24	1	186
HRAM1001HV	99999	3	99999	99999	80
HRAM1002HV	99999	0	99999	99999	37
HRAM1005HV	99999	2	99999	99999	83
HRAM1006HV	99999	2	99999	99999	136
HRAM1007HV	99999	0	99999	99999	85
HRAM1008HV	99999	1	99999	99999	56
HRAM1009HV	99999	1	99999	99999	23
HRAM1010HV	99999	2	99999	99999	119
HRAM1013HV	99999	2	99999	99999	64
HRAM1014HV	99999	0	99999	99999	145
HRAM1015HV	99999	0	99999	99999	39
HRAM1016HV	99999	1	99999	99999	80
HRAM1017HV	99999	2	99999	99999	57

ID	area_squeeze	profile_squeeze	new_endurance	area_endurance	profile_endurance
WPSS1006HV	360	252	43	1295	259.6
ASF1001HV	757	690.3	89	2667	535.8
ASF1002HV	1462	855	147	4537	634.4
ASF1003HV	331	481.9	44	1252	384
ASF1005HV	418	408.8	72	2184	367.2
ASF1013HV	478	697.5	79	2397	516.6
ASF1014HV	409	324	60	1858	206.4
ASF1016HV	540	477	17	535	236.5
ASF1017HV	875	561.6	109	3295	448.2
ASF1019HV	441	495	49	1488	402
ASF1021HV	721	733.2	88	2705	632
ASF1023HV	289	448	17	509	366
ASF1024HV	117	404.2	19	583	423
ASF1025HV	226	468	15	458	422.4
ASF1026HV	332	413.4	46	1373	385
ASF1030HV	174	170	12	350	190
ASF1032HV	1121	774.7	111	3342	490
ASF1033HV	676	987	84	2519	631.8
ASF1037HV	381	730.8	19	567	302.5
WPSS1040HV	174	392	45	1355	383.8
WPSS1032HV	420	473.2	37	1105	351.9
WPSS1031HV	1044	890.8	139	4180	743.4
WPSS1028HV	708	462.8	61	1819	421.2
WPSS1027HV	649	676	56	1691	480
WPSS1026HV	883	552	85	2560	365.8
WPSS1025HV	738	561.6	42	1267	244.2
WPSS1023HV	1237	811.2	208	6353	729.6
WPSS1022HV	882	455.7	59	1807	235.2
WPSS1020HV	816	499.8	78	2367	337.5
WPSS1018HV	587	486	47	1429	267.9
WPSS1017HV	1039	709.5	145	4395	546
WPSS1016HV	1132	1124.8	115	3453	824.9
WPSS1015HV	260	488.4	44	1325	392
WPSS1014HV	99	357.5	17	527	265.2
WPSS1043HV	182	351	43	1277	307.8
WPSS1045HV	948	969.4	143	4309	640.2
HRAM1001HV	454	368.9	50	1581	249
HRAM1002HV	220	264.6	16	482	193.2
HRAM1005HV	433	436.8	65	1957	371.3
HRAM1006HV	682	307.5	62	1874	195
HRAM1007HV	477	482.3	66	1979	421.4
HRAM1008HV	318	298.2	42	1245	279
HRAM1009HV	116	201.4	22	664	188.6
HRAM1010HV	597	416.5	36	1109	296.8
HRAM1013HV	321	384	27	806	348.8
HRAM1014HV	926	642.6	70	2098	415.8
HRAM1015HV	199	282.2	33	996	305.5
HRAM1016HV	541	504.9	34	1034	397.8
HRAM1017HV	286	257.6	30	893	253.7

ID	vaizey_group_6_16	rest_profile	line_rest	con_rest	new_rest	line_squeeze
WPSS1006HV	0	135.3	61	51	68	59
ASF1001HV	0	166.5	73	59	77	135
ASF1002HV	0	79.2	50	74	50	197
ASF1003HV	0	115.5	50	67	53	87
ASF1005HV	0	129.5	56	99999	57	118
ASF1013HV	0	181.5	79	99999	75	119
ASF1014HV	0	87	42	79	41	116
ASF1016HV	0	121.8	73	73	67	92
ASF1017HV	0	133.4	71	99999	70	202
ASF1019HV	0	112.2	44	99999	49	87
ASF1021HV	0	189	59	99999	57	124
ASF1023HV	0	211.5	77	99999	74	61
ASF1024HV	0	206.7	78	99999	97	52
ASF1025HV	0	296.8	76	99999	73	55
ASF1026HV	0	178.6	75	85	75	37
ASF1030HV	0	159.8	62	99999	60	52
ASF1032HV	0	171.5	70	99999	63	119
ASF1033HV	0	229.4	111	99999	102	94
ASF1037HV	0	188	67	99999	68	45
WPSS1040HV	0	241.8	92	99999	88	43
WPSS1032HV	0	252	93	35	90	56
WPSS1031HV	0	144.4	64	22	63	101
WPSS1028HV	0	167.2	56	58	53	50
WPSS1027HV	0	254.2	102	63	105	122
WPSS1026HV	0	157.5	51	46	51	125
WPSS1025HV	0	120.4	60	35	60	56
WPSS1023HV	0	94.5	46	22	48	43
WPSS1022HV	0	67.2	32	99999	31	134
WPSS1020HV	0	151.2	60	21	53	124
WPSS1018HV	0	169.2	86	47	84	119
WPSS1017HV	0	122.4	66	99999	65	69
WPSS1016HV	0	220.8	81	99999	79	100
WPSS1015HV	0	227.9	68	68	67	48
WPSS1014HV	0	227.9	73	99999	73	23
WPSS1043HV	0	113.1	39	39	39	45
WPSS1045HV	0	113.1	61	24	60	85
HRAM1001HV	0	151.8	61	99999	55	76
HRAM1002HV	0	175.5	64	99999	61	69
HRAM1005HV	0	167.2	69	99999	57	51
HRAM1006HV	0	87	43	99999	41	93
HRAM1007HV	0	220.8	82	99999	75	57
HRAM1008HV	0	162	49	99999	51	88
HRAM1009HV	0	113.4	66	99999	66	47
HRAM1010HV	0	137.2	68	99999	78	158
HRAM1013HV	0	227.5	98	99999	106	133
HRAM1014HV	0	180.4	59	99999	53	146
HRAM1015HV	0	151.7	49	99999	52	47
HRAM1016HV	0	202.8	90	99999	85	105
HRAM1017HV	0	140	66	99999	58	81

ID	Group	Sex	Age	Children	Symptoms	Urge_symptoms	External_muscle
HRAM1018HV	0	0	48	1	99999	99999	99999
HRAM1019HV	0	0	56	1	99999	99999	99999
HRAM1021HV	0	0	40	1	99999	99999	99999
HRAM1022HV	0	0	62	1	99999	99999	99999
HRAM1023HV	0	0	57	1	99999	99999	99999
HRAM1024HV	0	0	46	1	99999	99999	99999
HRAM1025HV	0	0	44	1	99999	99999	99999
HRAM1026HV	0	0	53	1	99999	99999	99999
HRAM1028HV	0	0	37	1	99999	99999	99999
HRAM1031HV	0	0	32	1	99999	99999	99999
HRAM1035HV	0	0	21	1	99999	99999	99999
HRAM1036HV	0	0	35	0	99999	99999	99999
HRAM1038HV	0	0	59	0	99999	99999	99999
HRAM1039HV	0	0	35	1	99999	99999	99999
HRAM1040HV	0	0	50	0	99999	99999	99999
HRAM1041HV	0	0	30	0	99999	99999	99999
HRAM1042HV	0	0	33	0	99999	99999	99999
HRAM1043HV	0	0	39	0	99999	99999	99999
HRAM1051HV	0	0	22	0	99999	99999	99999
HRAM1056HV	0	0	27	1	99999	99999	99999
HRAM1057HV	0	0	27	0	99999	99999	99999
HRAM1059HV	0	0	24	0	99999	99999	99999
HRAM1067HV	0	0	54	0	99999	99999	99999
HRAM1069HV	0	0	33	0	99999	99999	99999
HV006C	0	0	31	0	99999	99999	99999
HV007B	0	0	28	0	99999	99999	99999
HV008B	0	0	27	0	99999	99999	99999
HV012B	0	0	28	0	99999	99999	99999
HV012C	0	0	23	0	99999	99999	99999
HV013C	0	0	37	0	99999	99999	99999
HV014B	0	0	55	1	99999	99999	99999
HV015B	0	0	50	0	99999	99999	99999
HV015C	0	0	55	1	99999	99999	99999
HV016B	0	0	18	0	99999	99999	99999
HV017C	0	0	37	1	99999	99999	99999
HV019C	0	0	62	0	99999	99999	99999
ARP1001	1	0	65	1	1	0	0
ARP1002	1	0	44	1	1	1	1
ARP1003	1	0	36	0	1	0	0
ARP1004	1	0	77	1	1	1	1
ARP1008	1	0	77	1	1	0	0
ARP1012	1	0	51	1	1	1	1
ARP1013	1	0	69	1	1	1	1
ARP1014	1	0	45	0	1	1	0
ARP1015	1	0	71	1	1	1	1
ARP1016	1	0	32	1	1	1	1
ARP1017	1	0	56	1	1	1	1
ARP1019	1	0	67	1	1	1	1
ARP1023	1	0	60	1	1	1	0

ID	Internal_muscle	Vaizey_score	conventional_Sq	normal_convent	new_squeeze
HRAM1018HV	99999	0	99999	99999	177
HRAM1019HV	99999	3	99999	99999	151
HRAM1021HV	99999	4	99999	99999	88
HRAM1022HV	99999	2	99999	99999	112
HRAM1023HV	99999	2	99999	99999	140
HRAM1024HV	99999	0	99999	99999	60
HRAM1025HV	99999	1	99999	99999	143
HRAM1026HV	99999	1	99999	99999	93
HRAM1028HV	99999	0	99999	99999	86
HRAM1031HV	99999	1	99999	99999	125
HRAM1035HV	99999	0	99999	99999	125
HRAM1036HV	99999	2	99999	99999	92
HRAM1038HV	99999	1	99999	99999	109
HRAM1039HV	99999	3	99999	99999	168
HRAM1040HV	99999	1	99999	99999	227
HRAM1041HV	99999	0	99999	99999	233
HRAM1042HV	99999	2	99999	99999	59
HRAM1043HV	99999	1	99999	99999	216
HRAM1051HV	99999	2	99999	99999	27
HRAM1056HV	99999	0	99999	99999	116
HRAM1057HV	99999	1	99999	99999	54
HRAM1059HV	99999	0	99999	99999	182
HRAM1067HV	99999	2	99999	99999	204
HRAM1069HV	99999	0	99999	99999	80
HV006C	99999	2	99999	99999	130
HV007B	99999	3	99999	99999	86
HV008B	99999	1	99999	99999	60
HV012B	99999	3	99999	99999	109
HV012C	99999	3	99999	99999	154
HV013C	99999	3	99999	99999	274
HV014B	99999	3	117	0	271
HV015B	99999	3	152	0	154
HV015C	99999	3	99999	99999	106
HV016B	99999	3	99999	99999	163
HV017C	99999	3	99999	99999	195
HV019C	99999	3	99999	99999	155
ARP1001	1	9	93	0	3
ARP1002	1	18	150	0	33
ARP1003	0	15	39	0	28
ARP1004	0	16	36	0	21
ARP1008	0	12	32	1	21
ARP1012	0	9	44	0	29
ARP1013	1	21	31	1	3
ARP1014	0	16	14	1	8
ARP1015	1	14	11	1	-4
ARP1016	0	9	42	0	23
ARP1017	1	17	43	0	26
ARP1019	0	13	40	0	31
ARP1023	1	23	60	0	15

ID	area_squeeze	profile_squeeze	new_endurance	area_endurance	profile_endurance
HRAM1018HV	886	870	66	1994	451.2
HRAM1019HV	888	676.2	84	2555	474.3
HRAM1021HV	441	360.4	48	1433	282.9
HRAM1022HV	603	483.6	44	1323	288.1
HRAM1023HV	698	332.5	91	2664	268.8
HRAM1024HV	399	284.9	20	612	181.3
HRAM1025HV	729	380.8	63	1898	241.9
HRAM1026HV	463	269.7	41	1233	189
HRAM1028HV	504	525	68	2075	445.5
HRAM1031HV	663	349.8	80	2394	241.8
HRAM1035HV	689	600	60	1796	451.4
HRAM1036HV	489	382.7	41	1253	273.8
HRAM1038HV	546	358.8	39	1200	275.6
HRAM1039HV	841	666.4	41	1223	359.6
HRAM1040HV	1135	654	114	3419	390
HRAM1041HV	1163	720.8	133	3998	455
HRAM1042HV	293	408.1	13	398	313.5
HRAM1043HV	1168	683.7	126	3774	485
HRAM1051HV	136	185	28	827	208
HRAM1056HV	497	598.5	71	2129	450.3
HRAM1057HV	269	369	10	308	253
HRAM1059HV	930	798	134	4068	612
HRAM1067HV	1061	660.8	117	3603	429.3
HRAM1069HV	482	457.6	60	1793	327.6
HV006C	649	646.8	39	1197	465
HV007B	421	440.8	55	1639	307.8
HV008B	311	477.3	100	3024	558.8
HV012B	543	549.9	46	1369	402.9
HV012C	754	806	73	2205	569.6
HV013C	1370	1274	161	4913	990
HV014B	1382	904.8	158	4719	572
HV015B	786	750	65	1957	535.3
HV015C	539	806.4	52	1607	562.8
HV016B	831	684.4	113	3401	488
HV017C	975	815.4	96	2869	523.8
HV019C	762	704	69	2071	421.2
ARP1001	13	147.6	5	142	131.1
ARP1002	165	356.4	14	409	317.2
ARP1003	139	314.9	28	851	362.1
ARP1004	104	136.8	19	578	155.4
ARP1008	103	200.9	4	111	117.8
ARP1012	149	326.4	16	484	280.5
ARP1013	17	86.8	0	2	72.9
ARP1014	43	121.8	6	168	101.5
ARP1015	-19	260.1	-1	-23	252
ARP1016	114	197.8	19	585	171.5
ARP1017	152	141	4	114	90
ARP1019	168	132.6	31	168	132.6
ARP1023	76	54.6	20	605	80.6

ID	vaizey_group_6_16	rest_profile	line_rest	con_rest	new_rest	line_squeeze
HRAM1018HV	0	286	82	99999	58	95
HRAM1019HV	0	183.6	71	99999	73	148
HRAM1021HV	0	127.1	57	99999	58	119
HRAM1022HV	0	140	62	99999	70	111
HRAM1023HV	0	46.8	32	99999	29	108
HRAM1024HV	0	95.2	50	99999	52	89
HRAM1025HV	0	72.9	34	99999	33	95
HRAM1026HV	0	84	35	99999	42	73
HRAM1028HV	0	190.8	75	99999	58	109
HRAM1031HV	0	70.3	47	99999	45	96
HRAM1035HV	0	151.2	55	99999	57	90
HRAM1036HV	0	121.5	66	99999	64	80
HRAM1038HV	0	115.2	52	99999	52	105
HRAM1039HV	0	198	76	99999	75	124
HRAM1040HV	0	128	50	99999	49	166
HRAM1041HV	0	196.8	72	99999	68	127
HRAM1042HV	0	225	66	99999	59	64
HRAM1043HV	0	114.8	54	99999	47	119
HRAM1051HV	0	70.3	53	99999	54	41
HRAM1056HV	0	196.8	72	99999	61	65
HRAM1057HV	0	184.5	60	99999	53	79
HRAM1059HV	0	173.4	85	99999	80	162
HRAM1067HV	0	136.5	62	99999	56	234
HRAM1069HV	0	79.2	53	99999	50	114
HV006C	0	295.8	71	99999	67	89
HV007B	0	178.6	54	99999	47	73
HV008B	0	197.2	92	99999	99	86
HV012B	0	265.5	97	99999	93	128
HV012C	0	163.2	51	99999	47	86
HV013C	0	423.4	111	99999	104	191
HV014B	0	163.8	69	97	64	186
HV015B	0	314.9	120	137	108	128
HV015C	0	366	107	99999	102	108
HV016B	0	89.9	53	99999	51	142
HV017C	0	159.8	56	99999	58	212
HV019C	0	185	83	99999	87	171
ARP1001	1	73.6	32	24	28	75
ARP1002	2	220.4	105	70	97	80
ARP1003	1	256.5	88	126	82	45
ARP1004	2	77.5	37	18	35	40
ARP1008	1	89.9	45	74	40	46
ARP1012	1	165.6	66	76	68	83
ARP1013	2	58.8	43	24	41	35
ARP1014	2	113.1	79	66	73	16
ARP1015	1	275.4	102	132	100	0
ARP1016	1	122.4	55	54	50	47
ARP1017	2	96	45	82	42	47
ARP1019	1	78.4	52	44	44	42
ARP1023	2	27.3	26	29	24	45

ID	Group	Sex	Age	Children	Symptoms	Urge_symptoms	External_muscle
ARP1026	1	0	53	1	1	0	1
ARP1032	1	0	65	1	1	0	1
ARP1034	1	0	42	1	1	1	1
ARP1035	1	0	71	1	1	0	1
ARP1036	1	0	74	1	1	0	1
ARP1037	1	0	67	1	1	1	1
ARP1038	1	0	72	1	1	1	0
ARP1040	1	0	81	1	1	1	1
ARP1041	1	0	85	1	1	1	1
ARP1043	1	0	43	0	1	1	0
ARP1045	1	0	28	1	1	1	1
ARP1046	1	0	37	1	1	0	1
ARP1048	1	0	47	1	1	0	0
ARP1049	1	0	25	0	1	0	0
ARP1050	1	0	25	1	1	1	1
ARP1052	1	0	31	1	1	1	0
ARP1055	1	0	41	1	1	1	1
ARP1057	1	0	47	1	1	0	1
ARP1058	1	0	29	0	1	0	0
ARP1060	1	0	31	0	1	1	0
ARP1063	1	0	32	0	1	0	0
ARP1066	1	0	72	1	1	1	1
ARP1067	1	0	81	1	1	0	0
ARP1070	1	0	35	1	1	1	1
ARP1072	1	0	30	1	1	1	1
ARP1073	1	0	36	0	1	0	0
ARP1075	1	0	30	0	1	1	0
ARP1076	1	0	56	1	1	1	0
ARP1077	1	0	53	1	1	1	1
ARP1078	1	0	68	1	1	0	1
ARP1079	1	0	50	0	1	0	1
ARP1082	1	0	64	1	1	0	1
ARP1085	1	0	44	0	1	0	0
ARP1092	1	0	25	0	1	1	1
ARP1096	1	0	53	1	1	1	1
ARP1097	1	0	49	1	1	1	0
ARP1098	1	0	78	1	1	0	0
ARP1101	1	0	79	1	1	1	1
ARP1102	1	0	49	1	1	1	1
ARP1104	1	0	82	1	1	1	1
ARP1106	1	0	55	0	1	1	1
ARP1110	1	0	59	1	1	1	0
ARP1111	1	0	65	0	1	0	0
ARP1112	1	0	65	1	1	0	1
ARP2002	1	0	55	1	1	0	0
ARP2007	1	0	59	1	1	1	1
ARP2008	1	0	26	0	1	1	0
ARP2010	1	0	50	1	1	1	1
ARP2016	1	0	74	1	1	1	1

ID	Internal_muscle	Vaizey_score	conventional_Sq	normal_convent	new_squeeze
ARP1026	0	7	33	1	9
ARP1032	1	7	19	1	74
ARP1034	0	14	14	1	3
ARP1035	1	6	41	0	46
ARP1036	1	7	43	0	32
ARP1037	1	8	22	1	25
ARP1038	1	14	64	0	33
ARP1040	1	10	40	0	18
ARP1041	1	6	55	0	72
ARP1043	0	8	109	0	125
ARP1045	0	6	29	1	64
ARP1046	1	8	98	0	63
ARP1048	0	10	62	0	200
ARP1049	0	7	65	0	43
ARP1050	0	11	47	0	42
ARP1052	0	16	50	0	2
ARP1055	0	22	22	1	5
ARP1057	0	8	61	0	52
ARP1058	0	7	39	0	61
ARP1060	0	6	100	0	61
ARP1063	0	8	100	0	78
ARP1066	1	13	40	0	50
ARP1067	0	9	102	0	106
ARP1070	1	20	30	1	14
ARP1072	0	15	70	0	17
ARP1073	0	10	70	0	196
ARP1075	1	9	37	0	47
ARP1076	0	6	132	0	105
ARP1077	0	17	0	1	6
ARP1078	1	7	106	0	158
ARP1079	0	7	35	0	68
ARP1082	0	7	75	0	63
ARP1085	0	8	42	0	51
ARP1092	0	8	50	0	64
ARP1096	1	24	22	1	5
ARP1097	0	11	65	0	138
ARP1098	0	8	106	0	44
ARP1101	1	19	6	1	0
ARP1102	1	19	10	1	-3
ARP1104	0	16	22	1	17
ARP1106	1	11	120	0	144
ARP1110	0	9	20	1	44
ARP1111	0	10	168	0	232
ARP1112	1	19	66	0	123
ARP2002	0	13	99999	99999	238
ARP2007	1	19	99999	99999	47
ARP2008	0	8	99999	99999	88
ARP2010	1	6	22	1	3
ARP2016	1	13	24	1	11

ID	area_squeeze	profile_squeeze	new_endurance	area_endurance	profile_endurance
ARP1026	51	193.6	2	62	180.4
ARP1032	258	218.4	22	681	112.5
ARP1034	13	167.2	2	56	168.1
ARP1035	208	313.5	22	661	245
ARP1036	162	148.5	24	720	122.1
ARP1037	134	62.7	15	456	42
ARP1038	171	258.4	-1	-26	206.7
ARP1040	105	99.2	8	234	69.6
ARP1041	351	256	30	898	147
ARP1043	664	582.2	89	2727	489.9
ARP1045	335	277.2	36	1095	233.2
ARP1046	313	533.6	5	140	433.2
ARP1048	1101	709.5	63	1913	455.7
ARP1049	229	306.6	39	1288	278.4
ARP1050	224	372	18	527	270.9
ARP1052	8	233.7	13	404	265.5
ARP1055	26	117.6	3	82	85.1
ARP1057	263	347.1	24	725	296.4
ARP1058	316	460.6	32	973	367.2
ARP1060	304	248.2	76	2321	273.6
ARP1063	460	572.3	38	1133	398.4
ARP1066	311	252	30	896	197.4
ARP1067	540	626.4	26	791	415.8
ARP1070	72	150.5	2	56	150.4
ARP1072	81	227.7	13	397	191.1
ARP1073	1018	413.6	71	2171	220
ARP1075	247	368	-2	-46	282
ARP1076	630	455	52	1546	359.6
ARP1077	26	187	-3	-84	187.2
ARP1078	791	558.6	64	1918	359.6
ARP1079	341	286.2	58	1758	321.3
ARP1082	320	259.7	25	742	176
ARP1085	264	233.7	13	398	167.4
ARP1092	331	312	31	916	230
ARP1096	24	151.2	-9	-270	146.2
ARP1097	715	380.7	40	1231	249.6
ARP1098	239	285.2	28	844	269.8
ARP1101	1	37.2	0	15	29
ARP1102	-15	46.2	0	10	45.6
ARP1104	86	129.5	7	206	86.4
ARP1106	691	560	35	1062	374
ARP1110	222	290.4	12	363	173.6
ARP1111	1206	1020.3	110	3307	678.4
ARP1112	614	323.3	28	860	137.5
ARP2002	1093	489.1	81	2441	299.2
ARP2007	235	219	29	887	174.2
ARP2008	493	303.6	48	1496	230.3
ARP2010	13	52.7	2	63	42.5
ARP2016	73	40.8	8	245	35

ID	vaizey_group_6_16	rest_profile	line_rest	con_rest	new_rest	line_squeeze
ARP1026	1	162.8	82	48	79	23
ARP1032	1	59.4	24	34	19	115
ARP1034	1	192	62	61	53	10
ARP1035	1	148	68	52	64	102
ARP1036	1	65	38	46	35	47
ARP1037	1	36	0	22	52	27
ARP1038	1	190	88	50	86	48
ARP1040	1	52.7	23	42	24	44
ARP1041	1	70.2	39	33	37	98
ARP1043	1	69.6	35	62	35	85
ARP1045	1	189	108	71	89	72
ARP1046	1	259.7	93	111	100	76
ARP1048	1	268.4	103	96	98	113
ARP1049	1	132.6	50	70	49	66
ARP1050	1	210.7	83	106	73	80
ARP1052	2	218.4	96	100	94	22
ARP1055	2	68.2	33	51	30	35
ARP1057	1	154.8	93	92	92	80
ARP1058	1	247.5	82	65	76	75
ARP1060	1	110	74	66	69	105
ARP1063	1	272.6	115	88	97	105
ARP1066	1	107.5	44	40	44	84
ARP1067	1	330.6	76	93	73	95
ARP1070	2	144.3	81	90	78	27
ARP1072	1	173.6	88	99	88	39
ARP1073	1	91.8	41	100	38	123
ARP1075	1	216	80	118	81	67
ARP1076	1	159.1	74	60	84	106
ARP1077	2	178.2	93	116	87	0
ARP1078	1	91.8	55	45	42	125
ARP1079	1	128	59	54	63	68
ARP1082	1	48	38	34	38	93
ARP1085	1	107.3	47	61	55	82
ARP1092	1	148.2	65	68	62	70
ARP1096	2	125.4	67	92	62	18
ARP1097	1	136.5	69	118	64	40
ARP1098	1	185.6	99	83	99	182
ARP1101	2	42	26	24	26	6
ARP1102	2	57.5	45	15	44	0
ARP1104	2	44.8	26	40	29	40
ARP1106	1	215	78	107	77	226
ARP1110	1	156	87	107	87	72
ARP1111	1	260.4	108	146	101	202
ARP1112	2	31.2	14	41	13	126
ARP2002	1	92	31	99999	26	79
ARP2007	2	144	78	99999	76	78
ARP2008	1	124.7	65	99999	55	86
ARP2010	1	40	20	50	21	0
ARP2016	1	24	16	36	17	12

ID	Group	Sex	Age	Children	Symptoms	Urge_symptoms	External_muscle
ARP2022	1	0	64	1	1	1	1
ARP2024	1	0	51	1	1	0	1
ARP2025	1	0	62	1	1	1	0
ARP2026	1	0	30	0	1	0	0
ARP2028	1	0	50	1	1	0	1
ARP2035	1	0	35	1	1	1	1
ARP2039	1	0	70	1	1	0	1
3DVV1001PT	1	0	56	1	1	1	1
3DVV1002PT	1	0	64	1	1	1	1
3DVV1003PT	1	0	56	0	1	0	0
3DVV1006PT	1	0	27	1	1	1	1
3DVV1007PT	1	0	77	1	1	1	0
3DVV1008PT	1	0	73	0	1	0	0
3DVV1009PT	1	0	70	1	1	1	0
3DVV1011PT	1	0	56	1	1	1	1
3DVV1013PT	1	0	65	1	1	1	0
3DVV1014PT	1	0	50	1	1	1	1
3DVV1017PT	1	0	76	1	1	0	0
3DVV1018PT	1	0	56	1	1	0	0
3DVV1019PT	1	0	55	1	1	0	0
3DVV1020PT	1	0	78	1	1	1	1
ARP3006	1	0	51	1	1	1	1
ARP3008	1	0	69	1	1	1	1
ARP3009	1	0	44	1	1	1	0
ARP3010	1	0	37	1	1	1	0
ARP3011	1	0	60	0	1	1	0
ARP3012	1	0	77	1	1	0	1
ARP3013	1	0	48	1	1	0	0
ARP3014	1	0	61	1	1	0	1
ARP3015	1	0	48	1	1	1	1
ARP3016	1	0	77	1	1	1	1
ARP3017	1	0	59	1	1	1	1
ARP3019	1	0	60	1	1	1	1
M001	0	0	18	0	99999	99999	99999
M002	0	0	38	1	99999	99999	99999
M003	0	0	43	1	99999	99999	99999
M004	0	0	52	1	99999	99999	99999
M005	0	0	43	1	99999	99999	99999
M006	0	0	35	0	99999	99999	99999
M007	0	0	63	1	99999	99999	99999
M008	0	0	30	0	99999	99999	99999
M009	0	0	46	0	99999	99999	99999
M010	0	0	44	0	99999	99999	99999
M011	0	0	42	0	99999	99999	99999
M012	0	0	99999	0	99999	99999	99999
M013	0	0	34	1	99999	99999	99999
M014	0	0	55	1	99999	99999	99999
M015	0	0	99999	0	99999	99999	99999
M016	0	0	55	1	99999	99999	99999

ID	Internal_muscle	Vaizey_score	conventional_Sq	normal_convent	new_squeeze
ARP2022	1	10	36	0	22
ARP2024	0	13	99999	99999	0
ARP2025	1	19	20	1	59
ARP2026	0	9	132	0	45
ARP2028	0	10	99999	99999	22
ARP2035	1	11	16	1	19
ARP2039	0	10	99999	99999	109
3DVV1001PT	1	12	63	0	129
3DVV1002PT	1	11	21	1	8
3DVV1003PT	0	15	109	0	80
3DVV1006PT	1	11	43	0	38
3DVV1007PT	0	10	60	0	4
3DVV1008PT	0	13	37	1	12
3DVV1009PT	0	20	40	0	46
3DVV1011PT	0	11	40	0	29
3DVV1013PT	1	6	39	0	40
3DVV1014PT	0	11	33	1	14
3DVV1017PT	0	18	20	1	6
3DVV1018PT	1	17	47	0	62
3DVV1019PT	0	19	67	0	49
3DVV1020PT	1	11	26	1	8
ARP3006	0	10	99999	99999	2
ARP3008	0	15	99999	99999	11
ARP3009	0	20	99999	99999	5
ARP3010	1	15	99999	99999	40
ARP3011	0	14	99999	99999	52
ARP3012	1	10	99999	99999	35
ARP3013	1	15	99999	99999	71
ARP3014	1	15	99999	99999	83
ARP3015	1	14	99999	99999	28
ARP3016	1	12	99999	99999	89
ARP3017	1	14	99999	99999	41
ARP3019	1	8	99999	99999	30
M001	99999	99999	57	0	99999
M002	99999	99999	82	0	99999
M003	99999	99999	128	0	99999
M004	99999	99999	78	0	99999
M005	99999	99999	67	0	99999
M006	99999	99999	60	0	99999
M007	99999	99999	162	0	99999
M008	99999	99999	52	0	99999
M009	99999	99999	70	0	99999
M010	99999	99999	150	0	99999
M011	99999	99999	91	0	99999
M012	99999	99999	100	0	99999
M013	99999	99999	64	0	99999
M014	99999	99999	220	0	99999
M015	99999	99999	130	0	99999
M016	99999	99999	45	0	99999

ID	area_squeeze	profile_squeeze	new_endurance	area_endurance	profile_endurance
ARP2022	117	176.4	44	1339	171.6
ARP2024	-7	221.4	3	104	259.2
ARP2025	294	180.4	18	541	110.2
ARP2026	225	445.2	4	122	355.2
ARP2028	134	209	14	418	158.4
ARP2035	93	158.4	8	254	148.5
ARP2039	481	360	29	890	257.6
3DVV1001PT	763	180	105	3230	146.3
3DVV1002PT	46	73.5	9	265	102.4
3DVV1003PT	456	250.1	30	904	171
3DVV1006PT	224	114.4	16	487	102
3DVV1007PT	22	232.2	-2	-66	172
3DVV1008PT	79	64.4	12	388	62.4
3DVV1009PT	272	96	41	1255	115
3DVV1011PT	158	160	16	486	111.6
3DVV1013PT	205	170.5	8	237	133.3
3DVV1014PT	75	97.5	11	334	75
3DVV1017PT	41	100.8	10	299	88.4
3DVV1018PT	353	171	19	556	91
3DVV1019PT	248	283.2	24	725	193.2
3DVV1020PT	52	32.4	12	360	52.5
ARP3006	10	186	-10	-311	179.8
ARP3008	57	151.9	6	180	127.5
ARP3009	24	212	5	155	244.8
ARP3010	202	496.8	4	111	323.9
ARP3011	262	112.2	31	1056	135.2
ARP3012	170	91.8	15	458	67.6
ARP3013	354	676.5	18	539	439.9
ARP3014	407	190	28	853	100.7
ARP3015	138	367.5	9	270	282
ARP3016	445	572.4	28	813	413.1
ARP3017	212	189	36	1075	168
ARP3019	171	159.1	12	364	115
M001	99999	99999	99999	99999	99999
M002	99999	99999	99999	99999	99999
M003	99999	99999	99999	99999	99999
M004	99999	99999	99999	99999	99999
M005	99999	99999	99999	99999	99999
M006	99999	99999	99999	99999	99999
M007	99999	99999	99999	99999	99999
M008	99999	99999	99999	99999	99999
M009	99999	99999	99999	99999	99999
M010	99999	99999	99999	99999	99999
M011	99999	99999	99999	99999	99999
M012	99999	99999	99999	99999	99999
M013	99999	99999	99999	99999	99999
M014	99999	99999	99999	99999	99999
M015	99999	99999	99999	99999	99999
M016	99999	99999	99999	99999	99999

ID	vaizey_group_6_16	rest_profile	line_rest	con_rest	new_rest	line_squeeze
ARP2022	1	120.4	41	38	49	61
ARP2024	1	229.5	81	99999	83	43
ARP2025	2	76	24	63	22	58
ARP2026	1	405	106	29	110	23
ARP2028	1	151.8	84	99999	80	27
ARP2035	1	128.7	57	63	58	23
ARP2039	1	125.8	48	99999	48	128
3DVV1001PT	1	74.4	52	67	58	91
3DVV1002PT	1	57.5	33	46	24	17
3DVV1003PT	1	96.8	38	35	43	66
3DVV1006PT	1	62.4	31	68	30	32
3DVV1007PT	1	193.5	62	100	57	8
3DVV1008PT	1	18.2	15	46	14	42
3DVV1009PT	2	87.5	59	27	22	53
3DVV1011PT	1	100.8	40	66	38	42
3DVV1013PT	1	81	34	62	38	51
3DVV1014PT	1	28.8	22	75	22	46
3DVV1017PT	2	71.3	27	52	27	20
3DVV1018PT	2	57.6	33	63	32	93
3DVV1019PT	2	148.8	55	54	56	69
3DVV1020PT	1	15.3	14	29	15	26
ARP3006	1	167.4	81	99999	85	15
ARP3008	1	141.9	67	99999	66	25
ARP3009	2	140	64	99999	60	40
ARP3010	1	297.6	101	99999	101	64
ARP3011	1	74.4	43	99999	39	110
ARP3012	1	63.8	34	99999	32	62
ARP3013	1	404.7	100	99999	97	166
ARP3014	1	48.6	38	99999	37	97
ARP3015	1	259.2	86	99999	78	74
ARP3016	1	240	114	99999	110	170
ARP3017	1	50.4	29	99999	25	61
ARP3019	1	37.5	36	99999	33	95
M001	0	99999	99999	83	99999	99999
M002	0	99999	99999	96	99999	99999
M003	0	99999	99999	127	99999	99999
M004	0	99999	99999	70	99999	99999
M005	0	99999	99999	75	99999	99999
M006	0	99999	99999	80	99999	99999
M007	0	99999	99999	43	99999	99999
M008	0	99999	99999	77	99999	99999
M009	0	99999	99999	80	99999	99999
M010	0	99999	99999	77	99999	99999
M011	0	99999	99999	87	99999	99999
M012	0	99999	99999	60	99999	99999
M013	0	99999	99999	52	99999	99999
M014	0	99999	99999	76	99999	99999
M015	0	99999	99999	78	99999	99999
M016	0	99999	99999	35	99999	99999

ID	Group	Sex	Age	Children	Symptoms	Urge_symptoms	External_muscle
M017	0	0	38	0	99999	99999	99999
M018	0	0	45	1	99999	99999	99999
M019	0	0	18	0	99999	99999	99999
M020	0	0	27	0	99999	99999	99999
M021	0	0	25	0	99999	99999	99999
M022	0	0	51	1	99999	99999	99999
M023	0	0	34	0	99999	99999	99999
M024	0	0	53	1	99999	99999	99999
M025	0	0	43	1	99999	99999	99999
M026	0	0	50	1	99999	99999	99999
M027	0	0	50	1	99999	99999	99999
M028	0	0	60	1	99999	99999	99999
M029	0	0	34	0	99999	99999	99999
M030	0	0	26	0	99999	99999	99999
M031	0	0	25	0	99999	99999	99999
M032	0	0	41	1	99999	99999	99999
M033	0	0	58	0	99999	99999	99999
M034	0	0	27	0	99999	99999	99999
M035	0	0	52	1	99999	99999	99999
M036	0	0	49	1	99999	99999	99999
M037	0	0	42	0	99999	99999	99999
M038	0	0	52	1	99999	99999	99999
M039	0	0	22	0	99999	99999	99999
M040	0	0	62	0	99999	99999	99999
M041	0	0	43	1	99999	99999	99999
M042	0	0	54	1	99999	99999	99999
M043	0	0	49	1	99999	99999	99999
M044	0	0	57	1	99999	99999	99999
M045	0	0	30	0	99999	99999	99999
M046	0	0	45	1	99999	99999	99999
M047	0	0	18	0	99999	99999	99999
M048	0	0	25	0	99999	99999	99999
M049	0	0	26	0	99999	99999	99999
M050	0	0	57	1	99999	99999	99999

ID	Internal_muscle	Vaizey_score	conventional_Sq	normal_convent	new_squeeze
M017	99999	99999	100	0	99999
M018	99999	99999	78	0	99999
M019	99999	99999	59	0	99999
M020	99999	99999	135	0	99999
M021	99999	99999	150	0	99999
M022	99999	99999	200	0	99999
M023	99999	99999	70	0	99999
M024	99999	99999	56	0	99999
M025	99999	99999	247	0	99999
M026	99999	99999	190	0	99999
M027	99999	99999	135	0	99999
M028	99999	99999	107	0	99999
M029	99999	99999	65	0	99999
M030	99999	99999	208	0	99999
M031	99999	99999	54	0	99999
M032	99999	99999	53	0	99999
M033	99999	99999	120	0	99999
M034	99999	99999	100	0	99999
M035	99999	99999	107	0	99999
M036	99999	99999	48	0	99999
M037	99999	99999	145	0	99999
M038	99999	99999	47	0	99999
M039	99999	99999	100	0	99999
M040	99999	99999	25	0	99999
M041	99999	99999	49	0	99999
M042	99999	99999	167	0	99999
M043	99999	99999	87	0	99999
M044	99999	99999	45	0	99999
M045	99999	99999	55	0	99999
M046	99999	99999	83	0	99999
M047	99999	99999	71	0	99999
M048	99999	99999	140	0	99999
M049	99999	99999	45	0	99999
M050	99999	99999	69	0	99999

ID	area_squeeze	profile_squeeze	new_endurance	area_endurance	profile_endurance
M017	99999	99999	99999	99999	99999
M018	99999	99999	99999	99999	99999
M019	99999	99999	99999	99999	99999
M020	99999	99999	99999	99999	99999
M021	99999	99999	99999	99999	99999
M022	99999	99999	99999	99999	99999
M023	99999	99999	99999	99999	99999
M024	99999	99999	99999	99999	99999
M025	99999	99999	99999	99999	99999
M026	99999	99999	99999	99999	99999
M027	99999	99999	99999	99999	99999
M028	99999	99999	99999	99999	99999
M029	99999	99999	99999	99999	99999
M030	99999	99999	99999	99999	99999
M031	99999	99999	99999	99999	99999
M032	99999	99999	99999	99999	99999
M033	99999	99999	99999	99999	99999
M034	99999	99999	99999	99999	99999
M035	99999	99999	99999	99999	99999
M036	99999	99999	99999	99999	99999
M037	99999	99999	99999	99999	99999
M038	99999	99999	99999	99999	99999
M039	99999	99999	99999	99999	99999
M040	99999	99999	99999	99999	99999
M041	99999	99999	99999	99999	99999
M042	99999	99999	99999	99999	99999
M043	99999	99999	99999	99999	99999
M044	99999	99999	99999	99999	99999
M045	99999	99999	99999	99999	99999
M046	99999	99999	99999	99999	99999
M047	99999	99999	99999	99999	99999
M048	99999	99999	99999	99999	99999
M049	99999	99999	99999	99999	99999
M050	99999	99999	99999	99999	99999

ID	vaizey_group_6_16	rest_profile	line_rest	con_rest	new_rest	line_squeeze
M017	0	99999	99999	80	99999	99999
M018	0	99999	99999	59	99999	99999
M019	0	99999	99999	45	99999	99999
M020	0	99999	99999	93	99999	99999
M021	0	99999	99999	100	99999	99999
M022	0	99999	99999	85	99999	99999
M023	0	99999	99999	100	99999	99999
M024	0	99999	99999	94	99999	99999
M025	0	99999	99999	73	99999	99999
M026	0	99999	99999	110	99999	99999
M027	0	99999	99999	72	99999	99999
M028	0	99999	99999	81	99999	99999
M029	0	99999	99999	78	99999	99999
M030	0	99999	99999	98	99999	99999
M031	0	99999	99999	54	99999	99999
M032	0	99999	99999	50	99999	99999
M033	0	99999	99999	50	99999	99999
M034	0	99999	99999	80	99999	99999
M035	0	99999	99999	85	99999	99999
M036	0	99999	99999	75	99999	99999
M037	0	99999	99999	52	99999	99999
M038	0	99999	99999	68	99999	99999
M039	0	99999	99999	100	99999	99999
M040	0	99999	99999	48	99999	99999
M041	0	99999	99999	62	99999	99999
M042	0	99999	99999	68	99999	99999
M043	0	99999	99999	34	99999	99999
M044	0	99999	99999	93	99999	99999
M045	0	99999	99999	99	99999	99999
M046	0	99999	99999	34	99999	99999
M047	0	99999	99999	88	99999	99999
M048	0	99999	99999	60	99999	99999
M049	0	99999	99999	101	99999	99999
M050	0	99999	99999	55	99999	99999

Chapter 7 - Prolonged studies of anorectal function using high resolution anal manometry in healthy volunteers and patients with faecal incontinence: characteristics of transient anal sphincter relaxations

ID	TASRID	AC length	R resting time	O resting time	TASR	T pre/post meal	T time
ASF1001HV	ASF1001HV1O	4	0:30:40	01:36:23	1	O	1:59:07
ASF1001HV	ASF1001HV2O	4	0:30:40	01:36:23	2	O	2:06:43
ASF1001HV	ASF1001HV3O	4	0:30:40	01:36:23	3	O	2:17:06
ASF1001HV	ASF1001HV4O	4	0:30:40	01:36:23	4	O	2:18:43
ASF1001HV	ASF1001HV5O	4	0:30:40	01:36:23	5	O	2:19:43
ASF1005HV	ASF1005HV1R	3.6	00:29:17	01:48:52	1	R	0:43:34
ASF1005HV	ASF1005HV2O	3.6	00:29:17	01:48:52	2	O	2:18:16
ASF1007HV	ASF1007HV1O	3.9	00:25:24	02:03:13	1	O	2:03:58
ASF1007HV	ASF1007HV2O	3.9	00:25:24	02:03:13	2	O	2:07:29
ASF1007HV	ASF1007HV3O	3.9	00:25:24	02:03:13	3	O	2:09:12
ASF1007HV	ASF1007HV4O	3.9	00:25:24	02:03:13	4	O	2:12:47
ASF1007HV	ASF1007HV5O	3.9	00:25:24	02:03:13	5	O	2:17:10
ASF1010HV	ASF1010HV1R	4.7	00:28:18	01:39:07	1	R	0:56:22
ASF1010HV	ASF1010HV2O	4.7	00:28:18	01:39:07	2	O	1:47:16
ASF1010HV	ASF1010HV3O	4.7	00:28:18	01:39:07	3	O	1:53:16
ASF1010HV	ASF1010HV4O	4.7	00:28:18	01:39:07	4	O	1:56:41
ASF1010HV	ASF1010HV5O	4.7	00:28:18	01:39:07	5	O	1:57:23
ASF1010HV	ASF1010HV6O	4.7	00:28:18	01:39:07	6	O	2:04:37
ASF1010HV	ASF1010HV7O	4.7	00:28:18	01:39:07	7	O	2:20:56
ASF1011HV	ASF1011HV1R	3.5	00:23:50	01:47:10	1	R	1:02:20
ASF1011HV	ASF1011HV2R	3.5	00:23:50	01:47:10	2	R	1:09:01
ASF1011HV	ASF1011HV3O	3.5	00:23:50	01:47:10	3	O	2:31:36
ASF1012HV	ASF1012HV1R	3.9	00:23:57	01:39:59	1	R	2:09:33
ASF1013HV	ASF1013HV1O	3.2	01:13:22	02:39:21	1	O	2:41:14
ASF1013HV	ASF1013HV2O	3.2	01:13:22	02:39:21	2	O	2:57:01
ASF1013HV	ASF1013HV3O	3.2	01:13:22	02:39:21	3	O	3:00:53
ASF1014HV	ASF1014HV1R	3.4	00:25:13	01:38:52	1	R	0:33:02
ASF1014HV	ASF1014HV2R	3.4	00:25:13	01:38:52	2	R	0:40:10
ASF1014HV	ASF1014HV3R	3.4	00:25:13	01:38:52	3	R	1:10:12
ASF1014HV	ASF1014HV4O	3.4	00:25:13	01:38:52	4	O	1:39:06
ASF1014HV	ASF1014HV5O	3.4	00:25:13	01:38:52	5	O	1:39:36
ASF1014HV	ASF1014HV6O	3.4	00:25:13	01:38:52	6	O	1:40:38
ASF1014HV	ASF1014HV7O	3.4	00:25:13	01:38:52	7	O	1:41:04
ASF1014HV	ASF1014HV8O	3.4	00:25:13	01:38:52	8	O	1:41:39
ASF1014HV	ASF1014HV9O	3.4	00:25:13	01:38:52	9	O	1:42:07
ASF1014HV	ASF1014HV10O	3.4	00:25:13	01:38:52	10	O	1:42:51
ASF1014HV	ASF1014HV11O	3.4	00:25:13	01:38:52	11	O	1:45:31
ASF1014HV	ASF1014HV12O	3.4	00:25:13	01:38:52	12	O	1:46:16
ASF1014HV	ASF1014HV13O	3.4	00:25:13	01:38:52	13	O	1:47:00
ASF1014HV	ASF1014HV14O	3.4	00:25:13	01:38:52	14	O	1:47:50

ID	TASRID	AC length	R resting time	O resting time	TASR	T pre/post meal	T time
ASF1014HV	ASF1014HV15O	3.4	00:25:13	01:38:52	15	O	1:48:43
ASF1014HV	ASF1014HV16O	3.4	00:25:13	01:38:52	16	O	1:49:30
ASF1014HV	ASF1014HV17O	3.4	00:25:13	01:38:52	17	O	1:50:08
ASF1014HV	ASF1014HV18O	3.4	00:25:13	01:38:52	18	O	1:52:30
ASF1014HV	ASF1014HV19O	3.4	00:25:13	01:38:52	19	O	1:52:32
ASF1014HV	ASF1014HV20O	3.4	00:25:13	01:38:52	20	O	1:54:31
ASF1014HV	ASF1014HV21O	3.4	00:25:13	01:38:52	21	O	1:57:26
ASF1014HV	ASF1014HV22O	3.4	00:25:13	01:38:52	22	O	1:59:46
ASF1014HV	ASF1014HV23O	3.4	00:25:13	01:38:52	23	O	2:01:39
ASF1014HV	ASF1014HV24O	3.4	00:25:13	01:38:52	24	O	2:02:16
ASF1014HV	ASF1014HV25O	3.4	00:25:13	01:38:52	25	O	2:03:07
ASF1017HV	ASF1017HV1R	2.9	00:25:16	01:42:28	1	R	0:37:44
ASF1017HV	ASF1017HV2O	2.9	00:25:16	01:42:28	2	O	1:47:02
ASF1017HV	ASF1017HV3O	2.9	00:25:16	01:42:28	3	O	1:50:57
ASF1017HV	ASF1017HV4O	2.9	00:25:16	01:42:28	4	O	1:53:32
ASF1017HV	ASF1017HV5O	2.9	00:25:16	01:42:28	5	O	1:54:12
ASF1017HV	ASF1017HV6O	2.9	00:25:16	01:42:28	6	O	1:56:09
ASF1017HV	ASF1017HV7O	2.9	00:25:16	01:42:28	7	O	1:56:43
ASF1017HV	ASF1017HV8O	2.9	00:25:16	01:42:28	8	O	2:04:08
ASF1017HV	ASF1017HV9O	2.9	00:25:16	01:42:28	9	O	2:16:09
ASF1017HV	ASF1017HV10O	2.9	00:25:16	01:42:28	10	O	2:22:27
ASF1017HV	ASF1017HV11O	2.9	00:25:16	01:42:28	11	O	2:27:08
ASF1020HV	ASF1020HV1O	3.3	00:21:30	01:46:59	1	O	2:26:57
ASF1020HV	ASF1020HV2O	3.3	00:21:30	01:46:59	2	O	2:29:09
ASF1020HV	ASF1020HV3O	3.3	00:21:30	01:46:59	3	O	2:30:24
ASF1022HV	ASF1022HV1O	2.9	00:22:35	01:48:04	1	O	1:58:08
ASF1025HV	ASF1025HV1O	4.1	00:21:06	01:40:58	1	O	1:45:42
ASF1025HV	ASF1025HV2O	4.1	00:21:06	01:40:58	2	O	1:55:31
ASF1025HV	ASF1025HV3O	4.1	00:21:06	01:40:58	3	O	2:10:41
ASF1025HV	ASF1025HV4O	4.1	00:21:06	01:40:58	4	O	2:14:30
ASF1025HV	ASF1025HV5O	4.1	00:21:06	01:40:58	5	O	2:20:19
ASF1028HV	ASF1028HV1R	4.9	00:07:47	01:37:58	1	R	00:16:08
ASF1028HV	ASF1028HV2O	4.9	00:07:47	01:37:58	2	O	01:43:36
ASF1028HV	ASF1028HV3O	4.9	00:07:47	01:37:58	3	O	02:01:20
ASF1028HV	ASF1028HV4O	4.9	00:07:47	01:37:58	4	O	02:15:58
ASF1028HV	ASF1028HV5O	4.9	00:07:47	01:37:58	5	O	02:18:30
ASF1029HV	ASF1029HV1O	3.3	00:16:26	01:34:05	1	O	01:41:07
ASF1029HV	ASF1029HV2O	3.3	00:16:26	01:34:05	2	O	01:46:34
ASF1029HV	ASF1029HV3O	3.3	00:16:26	01:34:05	3	O	01:55:48
ASF1029HV	ASF1029HV4O	3.3	00:16:26	01:34:05	4	O	01:58:01
ASF1030HV	ASF1030HV1R	3.1	00:02:38	01:30:55	1	R	00:08:21
ASF1030HV	ASF1030HV2R	3.1	00:02:38	01:30:55	2	R	00:12:28
ASF1030HV	ASF1030HV3R	3.1	00:02:38	01:30:55	3	R	00:16:03
ASF1030HV	ASF1030HV4R	3.1	00:02:38	01:30:55	4	R	00:23:43
ASF1030HV	ASF1030HV5R	3.1	00:02:38	01:30:55	5	R	00:25:26

ID	TASRID	AC length	R resting time	O resting time	TASR	T pre/post meal	T time
ASF1030HV	ASF1030HV6R	3.1	00:02:38	01:30:55	6	R	00:28:40
ASF1030HV	ASF1030HV7R	3.1	00:02:38	01:30:55	7	R	00:29:38
ASF1030HV	ASF1030HV8R	3.1	00:02:38	01:30:55	8	R	00:32:42
ASF1030HV	ASF1030HV9R	3.1	00:02:38	01:30:55	9	R	00:39:05
ASF1030HV	ASF1030HV10R	3.1	00:02:38	01:30:55	10	R	00:40:48
ASF1030HV	ASF1030HV11R	3.1	00:02:38	01:30:55	11	R	00:43:35
ASF1030HV	ASF1030HV12O	3.1	00:02:38	01:30:55	12	O	01:36:07
ASF1030HV	ASF1030HV13O	3.1	00:02:38	01:30:55	13	O	01:37:57
ASF1030HV	ASF1030HV14O	3.1	00:02:38	01:30:55	14	O	01:39:52
ASF1030HV	ASF1030HV15O	3.1	00:02:38	01:30:55	15	O	01:41:46
ASF1030HV	ASF1030HV16O	3.1	00:02:38	01:30:55	16	O	01:44:42
ASF1030HV	ASF1030HV17O	3.1	00:02:38	01:30:55	17	O	01:48:23
ASF1030HV	ASF1030HV18O	3.1	00:02:38	01:30:55	18	O	01:58:36
ASF1030HV	ASF1030HV19O	3.1	00:02:38	01:30:55	19	O	01:59:56
ASF1030HV	ASF1030HV20O	3.1	00:02:38	01:30:55	20	O	02:01:36
ASF1030HV	ASF1030HV21O	3.1	00:02:38	01:30:55	21	O	02:05:53
ASF1030HV	ASF1030HV22O	3.1	00:02:38	01:30:55	22	O	02:07:58
ASF1030HV	ASF1030HV23O	3.1	00:02:38	01:30:55	23	O	02:10:14
ASF1030HV	ASF1030HV24O	3.1	00:02:38	01:30:55	24	O	02:13:17
ASF1030HV	ASF1030HV25O	3.1	00:02:38	01:30:55	25	O	02:15:00
ASF1031HV	ASF1031HV1R	3.9	00:14:59	01:37:14	1	R	00:25:29
ASF1031HV	ASF1031HV2R	3.9	00:14:59	01:37:14	2	R	00:44:11
ASF1031HV	ASF1031HV3O	3.9	00:14:59	01:37:14	3	O	02:02:41
ASF1031HV	ASF1031HV4O	3.9	00:14:59	01:37:14	4	O	02:05:52
ASF1031HV	ASF1031HV5O	3.9	00:14:59	01:37:14	5	O	02:21:47
ASF1032HV	ASF1032HV1R	3.7	00:15:53	02:18:54	1	R	00:42:36
ASF1032HV	ASF1032HV2R	3.7	00:15:53	02:18:54	2	R	00:48:14
ASF1032HV	ASF1032HV3R	3.7	00:15:53	02:18:54	3	R	00:55:39
ASF1032HV	ASF1032HV4O	3.7	00:15:53	02:18:54	4	O	02:22:50
ASF1032HV	ASF1032HV5O	3.7	00:15:53	02:18:54	5	O	02:25:59
ASF1032HV	ASF1032HV6O	3.7	00:15:53	02:18:54	6	O	02:39:33
ASF1032HV	ASF1032HV7O	3.7	00:15:53	02:18:54	7	O	02:42:25
ASF1032HV	ASF1032HV8O	3.7	00:15:53	02:18:54	8	O	02:44:41
ASF1032HV	ASF1032HV9O	3.7	00:15:53	02:18:54	9	O	02:47:18
ASF1032HV	ASF1032HV10O	3.7	00:15:53	02:18:54	10	O	02:55:08
ASF1032HV	ASF1032HV11O	3.7	00:15:53	02:18:54	11	O	02:57:51
ASF1033HV	ASF1033HV1R	3.6	00:15:32	01:48:22	1	R	00:31:46
ASF1033HV	ASF1033HV2R	3.6	00:15:32	01:48:22	2	R	00:44:04
ASF1033HV	ASF1033HV3R	3.6	00:15:32	01:48:22	3	R	00:46:40
ASF1033HV	ASF1033HV4R	3.6	00:15:32	01:48:22	4	R	00:51:03
ASF1033HV	ASF1033HV5O	3.6	00:15:32	01:48:22	5	O	01:52:05
ASF1033HV	ASF1033HV6O	3.6	00:15:32	01:48:22	6	O	01:58:54
ASF1037HV	ASF1037HV1O	3.1	00:00:00	00:00:01	1	O	00:06:39
ASF1037HV	ASF1037HV2R	3.6	00:15:32	01:48:22	2	R	00:31:13
ASF1037HV	ASF1037HV3R	3.6	00:15:32	01:48:22	3	R	00:35:09

ID	TASRID	AC length	R resting time	O resting time	TASR	T pre/post meal	T time
ASF1008HV	ASF1008HV1R	3.9	00:39:49	01:57:28	1	R	00:48:29
ASF1008HV	ASF1008HV2R	3.9	00:39:49	01:57:28	2	R	00:51:45
ASF1008HV	ASF1008HV3R	3.9	00:39:49	01:57:28	3	R	00:57:50
ASF1008HV	ASF1008HV4R	3.9	00:39:49	01:57:28	4	R	01:03:07
ASF1008HV	ASF1008HV5R	3.9	00:39:49	01:57:28	5	R	01:12:06
ASF1008HV	ASF1008HV6R	3.9	00:39:49	01:57:28	6	R	01:11:12
ASF1008HV	ASF1008HV7R	3.9	00:39:49	01:57:28	7	R	01:19:03
ASF1008HV	ASF1008HV8O	3.9	00:39:49	01:57:28	8	O	02:02:06
ASF1008HV	ASF1008HV9O	3.9	00:39:49	01:57:28	9	O	02:02:59
ASF1008HV	ASF1008HV10O	3.9	00:39:49	01:57:28	10	O	02:03:54
ASF1008HV	ASF1008HV11O	3.9	00:39:49	01:57:28	11	O	02:04:17
ASF1008HV	ASF1008HV12O	3.9	00:39:49	01:57:28	12	O	02:06:22
ASF1008HV	ASF1008HV13O	3.9	00:39:49	01:57:28	13	O	02:07:59
ASF1008HV	ASF1008HV14O	3.9	00:39:49	01:57:28	14	O	02:11:30
ASF1008HV	ASF1008HV15O	3.9	00:39:49	01:57:28	15	O	02:14:02
ASF1008HV	ASF1008HV16O	3.9	00:39:49	01:57:28	16	O	02:17:55
ASF1008HV	ASF1008HV17O	3.9	00:39:49	01:57:28	17	O	02:29:08
ASF1008HV	ASF1008HV18O	3.9	00:39:49	01:57:28	18	O	02:30:41
ASF1023HV	ASF1023HV1O	4.5	00:27:11	01:45:55	1	O	01:53:35
ASF1023HV	ASF1023HV2R	4.5	01:27:11	02:45:55	2	R	02:02:15
ASF1023HV	ASF1023HV3R	4.5	01:27:11	02:45:55	3	R	02:05:21
ASF1023HV	ASF1023HV4R	4.5	01:27:11	02:45:55	4	R	02:07:24
ASF1023HV	ASF1023HV5R	4.5	01:27:11	02:45:55	5	R	02:09:28
ASF1023HV	ASF1023HV6R	4.5	01:27:11	02:45:55	6	R	02:16:20
ASF1023HV	ASF1023HV7R	4.5	01:27:11	02:45:55	7	R	02:23:22
ASF1023HV	ASF1023HV8R	4.5	01:27:11	02:45:55	8	R	02:24:50
ASF1023HV	ASF1023HV9R	4.5	01:27:11	02:45:55	9	R	02:25:39
ASF1023HV	ASF1023HV10R	4.5	01:27:11	02:45:55	10	R	02:28:48
ASF1002HV	ASF1002HV1R	3.3	0:32:16	01:17:26	1	R	0:54:57
ASF1002HV	ASF1002HV2R	3.3	0:32:16	01:17:26	2	R	1:16:15
ASF1002HV	ASF1002HV3O	3.3	0:32:16	01:17:26	3	O	1:27:20
ASF1002HV	ASF1002HV4O	3.3	0:32:16	01:17:26	4	O	1:31:26
ASF1002HV	ASF1002HV5O	3.3	0:32:16	01:17:26	5	O	1:31:59
ASF1002HV	ASF1002HV6O	3.3	0:32:16	01:17:26	6	O	1:33:53
ASF1002HV	ASF1002HV7O	3.3	0:32:16	01:17:26	7	O	1:35:29
ASF1002HV	ASF1002HV8O	3.3	0:32:16	01:17:26	8	O	1:36:06
ASF1002HV	ASF1002HV9O	3.3	0:32:16	01:17:26	9	O	1:37:42
ASF1002HV	ASF1002HV10O	3.3	0:32:16	01:17:26	10	O	1:39:07
ASF1002HV	ASF1002HV11O	3.3	0:32:16	01:17:26	11	O	1:43:12
ASF1002HV	ASF1002HV12O	3.3	0:32:16	01:17:26	12	O	1:45:01
ASF1002HV	ASF1002HV13O	3.3	0:32:16	01:17:26	13	O	1:47:21
ASF1002HV	ASF1002HV14O	3.3	0:32:16	01:17:26	14	O	1:50:39
ASF1002HV	ASF1002HV15O	3.3	0:32:16	01:17:26	15	O	1:51:40
ASF1002HV	ASF1002HV16O	3.3	0:32:16	01:17:26	16	O	1:52:13
ASF1002HV	ASF1002HV17O	3.3	0:32:16	01:17:26	17	O	1:52:48

ID	TASRID	AC length	R resting time	O resting time	TASR	T pre/post meal	T time
ASF1002HV	ASF1002HV18O	3.3	0:32:16	01:17:26	18	O	1:53:13
ASF1002HV	ASF1002HV19O	3.3	0:32:16	01:17:26	19	O	1:54:54
ASF1002HV	ASF1002HV20O	3.3	0:32:16	01:17:26	20	O	1:55:43
ASF1002HV	ASF1002HV21O	3.3	0:32:16	01:17:26	21	O	1:56:40
ASF1002HV	ASF1002HV22O	3.3	0:32:16	01:17:26	22	O	1:57:20
ASF1002HV	ASF1002HV23O	3.3	0:32:16	01:17:26	23	O	1:59:44
ASF1002HV	ASF1002HV24O	3.3	0:32:16	01:17:26	24	O	2:02:13
ASF1002HV	ASF1002HV25O	3.3	0:32:16	01:17:26	25	O	2:02:52
ASF1002HV	ASF1002HV26O	3.3	0:32:16	01:17:26	26	O	2:03:44
ASF1002HV	ASF1002HV27O	3.3	0:32:16	01:17:26	27	O	2:04:05
ASF1002HV	ASF1002HV28O	3.3	0:32:16	01:17:26	28	O	2:05:02
ASF1002HV	ASF1002HV29O	3.3	0:32:16	01:17:26	29	O	2:06:10
ASF1002HV	ASF1002HV30O	3.3	0:32:16	01:17:26	30	O	2:06:38
ASF1002HV	ASF1002HV31O	3.3	0:32:16	01:17:26	31	O	2:07:35
ASF1002HV	ASF1002HV32O	3.3	0:32:16	01:17:26	32	O	2:12:34
ASF1002HV	ASF1002HV33O	3.3	0:32:16	01:17:26	33	O	2:13:38
ASF1002HV	ASF1002HV34O	3.3	0:32:16	01:17:26	34	O	2:14:13
ASF1002HV	ASF1002HV35O	3.3	0:32:16	01:17:26	35	O	2:15:45
ASF1002HV	ASF1002HV36O	3.3	0:32:16	01:17:26	36	O	2:16:54
ASF1002HV	ASF1002HV37O	3.3	0:32:16	01:17:26	37	O	2:18:31
ASF1002HV	ASF1002HV38O	3.3	0:32:16	01:17:26	38	O	2:19:11
ASF1002HV	ASF1002HV39O	3.3	0:32:16	01:17:26	39	O	2:19:57
ASF1002HV	ASF1002HV40O	3.3	0:32:16	01:17:26	40	O	2:23:49
ASF1002HV	ASF1002HV41O	3.3	0:32:16	01:17:26	41	O	2:24:50
ASF1002HV	ASF1002HV42O	3.3	0:32:16	01:17:26	42	O	2:25:26
ASF1002HV	ASF1002HV43O	3.3	0:32:16	01:17:26	43	O	2:27:44
ASF1002HV	ASF1002HV44O	3.3	0:32:16	01:17:26	44	O	2:28:55
ASF1002HV	ASF1002HV43O	3.3	0:32:16	01:17:26	43	O	2:29:51
ASF1002HV	ASF1002HV44O	3.3	0:32:16	01:17:26	44	O	2:32:14
ASF1002HV	ASF1002HV45O	3.3	0:32:16	01:17:26	45	O	2:33:17
ASF1002HV	ASF1002HV46O	3.3	0:32:16	01:17:26	46	O	2:33:46
ASF1002HV	ASF1002HV47O	3.3	0:32:16	01:17:26	47	O	2:35:28

ID	TASRID	T Occurance	T perception	T perception type	T score	T duration
ASF1001HV	ASF1001HV1O	0:22:44	1	1	4	20
ASF1001HV	ASF1001HV2O	0:30:20	1	1	3	8
ASF1001HV	ASF1001HV3O	0:40:43	1	3	3	19
ASF1001HV	ASF1001HV4O	0:42:20	1	1	3	21
ASF1001HV	ASF1001HV5O	0:43:20	1	1	3	22
ASF1005HV	ASF1005HV1R	0:14:17	0	0	0	27
ASF1005HV	ASF1005HV2O	0:29:24	1	2	3	25
ASF1007HV	ASF1007HV1O	0:00:45	1	1	3	25
ASF1007HV	ASF1007HV2O	0:04:16	1	1	10	28
ASF1007HV	ASF1007HV3O	0:05:59	1	1	10	10
ASF1007HV	ASF1007HV4O	0:09:34	1	1	3	31
ASF1007HV	ASF1007HV5O	0:13:57	0	0	0	32
ASF1010HV	ASF1010HV1R	0:28:04	0	0	0	39
ASF1010HV	ASF1010HV2O	0:08:09	0	0	0	47
ASF1010HV	ASF1010HV3O	0:14:09	0	0	0	27
ASF1010HV	ASF1010HV4O	0:17:34	0	0	0	31
ASF1010HV	ASF1010HV5O	0:18:16	0	0	0	31
ASF1010HV	ASF1010HV6O	0:25:30	0	0	0	16
ASF1010HV	ASF1010HV7O	0:41:49	0	0	0	35
ASF1011HV	ASF1011HV1R	0:38:30	0	0	0	36
ASF1011HV	ASF1011HV2R	0:45:11	1	2	5	50
ASF1011HV	ASF1011HV3O	0:44:26	0	0	0	35
ASF1012HV	ASF1012HV1R	1:45:36	0	0	0	32
ASF1013HV	ASF1013HV1O	0:01:53	1	1	3	50
ASF1013HV	ASF1013HV2O	0:17:40	0	0	0	53
ASF1013HV	ASF1013HV3O	0:21:32	1	2	3	49
ASF1014HV	ASF1014HV1R	0:07:49	0	0	0	31
ASF1014HV	ASF1014HV2R	0:14:57	0	0	0	14
ASF1014HV	ASF1014HV3R	0:44:59	1	2	5	25
ASF1014HV	ASF1014HV4O	0:00:14	0	0	0	16
ASF1014HV	ASF1014HV5O	0:00:44	0	0	0	12
ASF1014HV	ASF1014HV6O	0:01:46	1	2	4	14
ASF1014HV	ASF1014HV7O	0:02:12	1	2	4	20
ASF1014HV	ASF1014HV8O	0:02:47	1	2	4	17
ASF1014HV	ASF1014HV9O	0:03:15	1	2	4	15
ASF1014HV	ASF1014HV10O	0:03:59	0	0	0	13
ASF1014HV	ASF1014HV11O	0:06:39	0	0	0	23
ASF1014HV	ASF1014HV12O	0:07:24	0	0	0	17
ASF1014HV	ASF1014HV13O	0:08:08	0	0	0	24
ASF1014HV	ASF1014HV14O	0:08:58	0	0	0	26

ID	TASRID	T Occurance	T perception	T perception type	T score	T duration
ASF1014HV	ASF1014HV15O	0:09:51	0	0	0	17
ASF1014HV	ASF1014HV16O	0:10:38	0	0	0	18
ASF1014HV	ASF1014HV17O	0:11:16	0	0	0	15
ASF1014HV	ASF1014HV18O	0:13:38	0	0	0	32
ASF1014HV	ASF1014HV19O	0:13:40	0	0	0	28
ASF1014HV	ASF1014HV20O	0:15:39	1	2	3	45
ASF1014HV	ASF1014HV21O	0:18:34	0	0	0	25
ASF1014HV	ASF1014HV22O	0:20:54	1	2	3	20
ASF1014HV	ASF1014HV23O	0:22:47	1	2	6	24
ASF1014HV	ASF1014HV24O	0:23:24	1	2	6	24
ASF1014HV	ASF1014HV25O	0:24:15	1	2	6	23
ASF1017HV	ASF1017HV1R	0:12:28	1	1	3	30
ASF1017HV	ASF1017HV2O	0:04:34	0	0	0	19
ASF1017HV	ASF1017HV3O	0:08:29	0	0	0	15
ASF1017HV	ASF1017HV4O	0:11:04	0	0	0	17
ASF1017HV	ASF1017HV5O	0:11:44	0	0	0	21
ASF1017HV	ASF1017HV6O	0:13:41	1	1	4	23
ASF1017HV	ASF1017HV7O	0:14:15	1	1	6	21
ASF1017HV	ASF1017HV8O	0:21:40	0	0	0	20
ASF1017HV	ASF1017HV9O	0:33:41	1	1	3	24
ASF1017HV	ASF1017HV10O	0:39:59	1	1	5	19
ASF1017HV	ASF1017HV11O	0:44:40	1	1	4	19
ASF1020HV	ASF1020HV1O	0:39:58	1	1	3.6	24
ASF1020HV	ASF1020HV2O	0:42:10	1	1	1.5	28
ASF1020HV	ASF1020HV3O	0:43:25	1	1	3.9	103
ASF1022HV	ASF1022HV1O	0:10:04	0	0	0	42
ASF1025HV	ASF1025HV1O	0:04:44	0	0	0	60
ASF1025HV	ASF1025HV2O	0:14:33	0	0	0	70
ASF1025HV	ASF1025HV3O	0:29:43	0	0	0	40
ASF1025HV	ASF1025HV4O	0:33:32	0	0	0	33
ASF1025HV	ASF1025HV5O	0:39:21	0	0	0	32
ASF1028HV	ASF1028HV1R	0:08:21	0	0	0	62
ASF1028HV	ASF1028HV2O	0:05:38	0	0	0	15
ASF1028HV	ASF1028HV3O	0:23:22	0	0	0	12
ASF1028HV	ASF1028HV4O	0:38:00	0	0	0	10
ASF1028HV	ASF1028HV5O	0:40:32	0	0	0	10
ASF1029HV	ASF1029HV1O	0:07:02	0	0	0	25
ASF1029HV	ASF1029HV2O	0:12:29	0	0	0	18
ASF1029HV	ASF1029HV3O	0:21:43	0	0	0	16
ASF1029HV	ASF1029HV4O	0:23:56	0	0	0	12
ASF1030HV	ASF1030HV1R	0:05:43	0	0	0	25
ASF1030HV	ASF1030HV2R	0:09:50	0	0	0	25
ASF1030HV	ASF1030HV3R	0:13:25	0	0	0	21
ASF1030HV	ASF1030HV4R	0:21:05	0	0	0	22
ASF1030HV	ASF1030HV5R	0:22:48	0	0	0	22

ID	TASRID	T Occurance	T perception	T perception type	T score	T duration
ASF1030HV	ASF1030HV6R	0:26:02	0	0	0	23
ASF1030HV	ASF1030HV7R	0:27:00	0	0	0	18
ASF1030HV	ASF1030HV8R	0:30:04	0	0	0	27
ASF1030HV	ASF1030HV9R	0:36:27	1	1	3	17
ASF1030HV	ASF1030HV10R	0:38:10	0	0	0	21
ASF1030HV	ASF1030HV11R	0:40:57	0	0	0	24
ASF1030HV	ASF1030HV12O	0:05:12	0	0	0	24
ASF1030HV	ASF1030HV13O	0:07:02	0	0	0	26
ASF1030HV	ASF1030HV14O	0:08:57	0	0	0	24
ASF1030HV	ASF1030HV15O	0:10:51	0	0	0	27
ASF1030HV	ASF1030HV16O	0:13:47	0	0	0	24
ASF1030HV	ASF1030HV17O	0:17:28	0	0	0	30
ASF1030HV	ASF1030HV18O	0:27:41	0	0	0	20
ASF1030HV	ASF1030HV19O	0:29:01	0	0	0	26
ASF1030HV	ASF1030HV20O	0:30:41	0	0	0	31
ASF1030HV	ASF1030HV21O	0:34:58	0	0	0	28
ASF1030HV	ASF1030HV22O	0:37:03	0	0	0	33
ASF1030HV	ASF1030HV23O	0:39:19	0	0	0	30
ASF1030HV	ASF1030HV24O	0:42:22	0	0	0	24
ASF1030HV	ASF1030HV25O	0:44:05	0	0	0	24
ASF1031HV	ASF1031HV1R	0:10:30	0	0	0	38
ASF1031HV	ASF1031HV2R	0:29:12	1	1	1.8	41
ASF1031HV	ASF1031HV3O	0:25:27	0	0	0	54
ASF1031HV	ASF1031HV4O	0:28:38	0	0	0	17
ASF1031HV	ASF1031HV5O	0:44:33	0	0	0	53
ASF1032HV	ASF1032HV1R	0:26:43	0	0	0	23
ASF1032HV	ASF1032HV2R	0:32:21	0	0	0	58
ASF1032HV	ASF1032HV3R	0:39:46	0	0	0	57
ASF1032HV	ASF1032HV4O	0:03:56	0	0	0	19
ASF1032HV	ASF1032HV5O	0:07:05	0	0	0	19
ASF1032HV	ASF1032HV6O	0:20:39	0	0	0	27
ASF1032HV	ASF1032HV7O	0:23:31	0	0	0	25
ASF1032HV	ASF1032HV8O	0:25:47	0	0	0	34
ASF1032HV	ASF1032HV9O	0:28:24	0	0	0	24
ASF1032HV	ASF1032HV10O	0:36:14	1	1	5	41
ASF1032HV	ASF1032HV11O	0:38:57	0	0	0	35
ASF1033HV	ASF1033HV1R	0:16:14	1	1	9.7	40
ASF1033HV	ASF1033HV2R	0:28:32	1	1	8.7	21
ASF1033HV	ASF1033HV3R	0:31:08	0	0	0	10
ASF1033HV	ASF1033HV4R	0:35:31	0	0	0	18
ASF1033HV	ASF1033HV5O	0:03:43	0	0	0	26
ASF1033HV	ASF1033HV6O	0:10:32	0	0	0	25
ASF1037HV	ASF1037HV1O	0:06:38	0	0	0	14
ASF1037HV	ASF1037HV2R	0:15:41	0	0	0	20
ASF1037HV	ASF1037HV3R	0:19:37	0	0	0	32

ID	TASRID	T Occurance	T perception	T perception type	T score	T duration
ASF1008HV	ASF1008HV1R	0:08:40	1	2	2	25
ASF1008HV	ASF1008HV2R	0:11:56	1	2	2	21
ASF1008HV	ASF1008HV3R	0:18:01	1	2	3	32
ASF1008HV	ASF1008HV4R	0:23:18	1	2	3	36
ASF1008HV	ASF1008HV5R	0:32:17	1	2	4	43
ASF1008HV	ASF1008HV6R	0:31:23	0	0	0	27
ASF1008HV	ASF1008HV7R	0:39:14	1	2	3	32
ASF1008HV	ASF1008HV8O	0:04:38	1	2	3	20
ASF1008HV	ASF1008HV9O	0:05:31	1	2	3	22
ASF1008HV	ASF1008HV10O	0:06:26	1	1	3	23
ASF1008HV	ASF1008HV11O	0:06:49	1	2	4	21
ASF1008HV	ASF1008HV12O	0:08:54	1	2	4	40
ASF1008HV	ASF1008HV13O	0:10:31	1	1	4	28
ASF1008HV	ASF1008HV14O	0:14:02	1	1	4	46
ASF1008HV	ASF1008HV15O	0:16:34	1	1	10	10
ASF1008HV	ASF1008HV16O	0:20:27	1	1	3	20
ASF1008HV	ASF1008HV17O	0:31:40	1	1	2	14
ASF1008HV	ASF1008HV18O	0:33:13	1	1	3	18
ASF1023HV	ASF1023HV1O	0:07:40	1	1	2.7	16
ASF1023HV	ASF1023HV2R	0:35:04	1	1	3	19
ASF1023HV	ASF1023HV3R	0:38:10	0	0	0	37
ASF1023HV	ASF1023HV4R	0:40:13	1	1	4	22
ASF1023HV	ASF1023HV5R	0:42:17	0	0	0	14
ASF1023HV	ASF1023HV6R	0:49:09	1	1	2.5	25
ASF1023HV	ASF1023HV7R	0:56:11	0	0	0	21
ASF1023HV	ASF1023HV8R	0:57:39	0	0	0	17
ASF1023HV	ASF1023HV9R	0:58:28	1	1	6.1	61
ASF1023HV	ASF1023HV10R	1:01:37	1	2	7	34
ASF1002HV	ASF1002HV1R	0:22:41	0	0	0	21
ASF1002HV	ASF1002HV2R	0:43:59	0	0	0	11
ASF1002HV	ASF1002HV3O	0:09:54	0	0	0	21
ASF1002HV	ASF1002HV4O	0:14:00	0	0	0	23
ASF1002HV	ASF1002HV5O	0:14:33	0	0	0	14
ASF1002HV	ASF1002HV6O	0:16:27	0	0	0	22
ASF1002HV	ASF1002HV7O	0:18:03	0	0	0	22
ASF1002HV	ASF1002HV8O	0:18:40	1	1	5	22
ASF1002HV	ASF1002HV9O	0:20:16	0	0	0	17
ASF1002HV	ASF1002HV10O	0:21:41	1	1	10	17
ASF1002HV	ASF1002HV11O	0:25:46	1	1	8	44
ASF1002HV	ASF1002HV12O	0:27:35	1	4	7	25
ASF1002HV	ASF1002HV13O	0:29:55	1	1	6	25
ASF1002HV	ASF1002HV14O	0:33:13	1	1	6	17
ASF1002HV	ASF1002HV15O	0:34:14	1	1	6	28
ASF1002HV	ASF1002HV16O	0:34:47	1	2	2	23
ASF1002HV	ASF1002HV17O	0:35:22	1	1	8	14

ID	TASRID	T Occurance	T perception	T perception type	T score	T duration
ASF1002HV	ASF1002HV18O	0:35:47	1	1	9	18
ASF1002HV	ASF1002HV19O	0:37:28	1	1	7	28
ASF1002HV	ASF1002HV20O	0:38:17	1	1	9	25
ASF1002HV	ASF1002HV21O	0:39:14	1	1	9	21
ASF1002HV	ASF1002HV22O	0:39:54	1	1	9	23
ASF1002HV	ASF1002HV23O	0:42:18	1	1	7	19
ASF1002HV	ASF1002HV24O	0:44:47	1	1	9	20
ASF1002HV	ASF1002HV25O	0:45:26	1	1	10	19
ASF1002HV	ASF1002HV26O	0:46:18	1	1	7	17
ASF1002HV	ASF1002HV27O	0:46:39	1	1	5	21
ASF1002HV	ASF1002HV28O	0:47:36	1	2	3	13
ASF1002HV	ASF1002HV29O	0:48:44	1	1	3	16
ASF1002HV	ASF1002HV30O	0:49:12	1	1	3	23
ASF1002HV	ASF1002HV31O	0:50:09	1	1	6	19
ASF1002HV	ASF1002HV32O	0:55:08	1	1	3	28
ASF1002HV	ASF1002HV33O	0:56:12	1	1	5	21
ASF1002HV	ASF1002HV34O	0:56:47	1	1	6	16
ASF1002HV	ASF1002HV35O	0:58:19	1	1	7	23
ASF1002HV	ASF1002HV36O	0:59:28	1	2	3	25
ASF1002HV	ASF1002HV37O	1:01:05	1	1	7	23
ASF1002HV	ASF1002HV38O	1:01:45	1	1	7	20
ASF1002HV	ASF1002HV39O	1:02:31	1	1	3	19
ASF1002HV	ASF1002HV40O	1:06:23	1	1	7	26
ASF1002HV	ASF1002HV41O	1:07:24	1	1	7	22
ASF1002HV	ASF1002HV42O	1:08:00	0	0	0	21
ASF1002HV	ASF1002HV43O	1:10:18	1	1	9	27
ASF1002HV	ASF1002HV44O	1:11:29	0	0	0	23
ASF1002HV	ASF1002HV43O	1:12:25	1	2	5	21
ASF1002HV	ASF1002HV44O	1:14:48	1	1	7	21
ASF1002HV	ASF1002HV45O	1:15:51	0	0	0	24
ASF1002HV	ASF1002HV46O	1:16:20	0	0	0	23
ASF1002HV	ASF1002HV47O	1:18:02	1	2	4	26

ID	TASRID	T depth cm	T depth %	Rectal Pressure Before	Ave Anal Pressure Before
ASF1001HV	ASF1001HV1O	2.1	0.53	25.60	68.60
ASF1001HV	ASF1001HV2O	1.1	0.28	27.40	65.20
ASF1001HV	ASF1001HV3O	1.5	0.38	25.00	76.80
ASF1001HV	ASF1001HV4O	1.1	0.28	27.80	82.80
ASF1001HV	ASF1001HV5O	0.8	0.20	28.20	79.80
ASF1005HV	ASF1005HV1R	2.1	0.58	12.25	52.00
ASF1005HV	ASF1005HV2O	2.3	0.64	16.00	49.60
ASF1007HV	ASF1007HV1O	3	0.77	37.17	47.50
ASF1007HV	ASF1007HV2O	3.9	1.00	42.80	48.25
ASF1007HV	ASF1007HV3O	3.9	1.00	31.67	62.50
ASF1007HV	ASF1007HV4O	1.6	0.41	36.80	63.00
ASF1007HV	ASF1007HV5O	2.2	0.56	36.83	61.75
ASF1010HV	ASF1010HV1R	1.7	0.36	17.50	109.00
ASF1010HV	ASF1010HV2O	1	0.21	14.00	82.50
ASF1010HV	ASF1010HV3O	1.4	0.30	9.67	90.50
ASF1010HV	ASF1010HV4O	1.2	0.26	10.00	93.00
ASF1010HV	ASF1010HV5O	1	0.21	15.00	89.00
ASF1010HV	ASF1010HV6O	1	0.21	10.00	66.67
ASF1010HV	ASF1010HV7O	1.7	0.36	13.00	71.50
ASF1011HV	ASF1011HV1R	1.2	0.34	43.25	99.80
ASF1011HV	ASF1011HV2R	2	0.57	49.67	110.80
ASF1011HV	ASF1011HV3O	2.5	0.71	39.25	88.80
ASF1012HV	ASF1012HV1R	1.6	0.41	17.40	75.40
ASF1013HV	ASF1013HV1O	1.7	0.53	29.00	63.20
ASF1013HV	ASF1013HV2O	2.1	0.66	30.25	68.60
ASF1013HV	ASF1013HV3O	1.8	0.56	21.00	66.60
ASF1014HV	ASF1014HV1R	1.2	0.35	13.25	52.40
ASF1014HV	ASF1014HV2R	1.5	0.44	17.25	56.50
ASF1014HV	ASF1014HV3R	1.4	0.41	12.60	55.00
ASF1014HV	ASF1014HV4O	2.2	0.65	14.75	46.50
ASF1014HV	ASF1014HV5O	2.2	0.65	20.00	51.60
ASF1014HV	ASF1014HV6O	2.2	0.65	17.25	32.00
ASF1014HV	ASF1014HV7O	2.2	0.65	17.75	45.40
ASF1014HV	ASF1014HV8O	2.3	0.68	17.25	45.60
ASF1014HV	ASF1014HV9O	2.3	0.68	23.00	54.80
ASF1014HV	ASF1014HV10O	2.1	0.62	18.50	54.20
ASF1014HV	ASF1014HV11O	2	0.59	18.75	40.00
ASF1014HV	ASF1014HV12O	1.8	0.53	17.25	38.40
ASF1014HV	ASF1014HV13O	1.9	0.56	20.25	49.80
ASF1014HV	ASF1014HV14O	1.8	0.53	23.25	62.00

ID	TASRID	T depth cm	T depth %	Rectal Pressure Before	Ave Anal Pressure Before
ASF1014HV	ASF1014HV15O	1.8	0.53	22.75	48.50
ASF1014HV	ASF1014HV16O	1.8	0.53	18.25	44.50
ASF1014HV	ASF1014HV17O	1.9	0.56	17.50	38.75
ASF1014HV	ASF1014HV18O	1.4	0.41	18.20	44.67
ASF1014HV	ASF1014HV19O	1.6	0.47	19.00	49.00
ASF1014HV	ASF1014HV20O	1.6	0.47	19.40	46.25
ASF1014HV	ASF1014HV21O	1.6	0.47	17.40	49.25
ASF1014HV	ASF1014HV22O	1.5	0.44	31.40	51.50
ASF1014HV	ASF1014HV23O	1.5	0.44	24.20	43.50
ASF1014HV	ASF1014HV24O	1.5	0.44	24.60	47.25
ASF1014HV	ASF1014HV25O	1.5	0.44	24.00	48.25
ASF1017HV	ASF1017HV1R	1.1	0.38	24.60	61.00
ASF1017HV	ASF1017HV2O	2.2	0.76	22.40	57.00
ASF1017HV	ASF1017HV3O	0.7	0.24	22.83	64.67
ASF1017HV	ASF1017HV4O	0.9	0.31	21.85	65.33
ASF1017HV	ASF1017HV5O	0.7	0.24	23.00	71.00
ASF1017HV	ASF1017HV6O	1.8	0.62	21.50	65.00
ASF1017HV	ASF1017HV7O	2.7	0.93	27.17	67.33
ASF1017HV	ASF1017HV8O	0.8	0.28	25.83	75.00
ASF1017HV	ASF1017HV9O	2.4	0.83	18.00	53.00
ASF1017HV	ASF1017HV10O	1.6	0.55	26.17	63.50
ASF1017HV	ASF1017HV11O	1.5	0.52	25.67	69.67
ASF1020HV	ASF1020HV1O	1.8	0.55	13.83	39.75
ASF1020HV	ASF1020HV2O	1.1	0.33	17.83	73.25
ASF1020HV	ASF1020HV3O	1.6	0.48	18.00	67.50
ASF1022HV	ASF1022HV1O	1.1	0.38	31.33	91.67
ASF1025HV	ASF1025HV1O	1.4	0.34	24.20	76.80
ASF1025HV	ASF1025HV2O	1.9	0.46	25.60	74.80
ASF1025HV	ASF1025HV3O	1.9	0.46	22.00	66.20
ASF1025HV	ASF1025HV4O	2.3	0.56	20.80	54.40
ASF1025HV	ASF1025HV5O	2.1	0.51	20.20	56.60
ASF1028HV	ASF1028HV1R	1.4	0.29	20.75	38.8
ASF1028HV	ASF1028HV2O	2.6	0.53	29.5	53
ASF1028HV	ASF1028HV3O	2.2	0.45	30	53.6
ASF1028HV	ASF1028HV4O	2.3	0.47	28.25	50.8
ASF1028HV	ASF1028HV5O	2.2	0.45	32.25	52.2
ASF1029HV	ASF1029HV1O	1	0.30	21.42857143	48.66666667
ASF1029HV	ASF1029HV2O	1.5	0.45	18.5	46
ASF1029HV	ASF1029HV3O	2.4	0.73	18.33333333	36.66666667
ASF1029HV	ASF1029HV4O	1.1	0.33	23.16666667	43.33333333
ASF1030HV	ASF1030HV1R	2	0.65	30.33333333	66.25
ASF1030HV	ASF1030HV2R	1.7	0.55	42.4	72.75
ASF1030HV	ASF1030HV3R	2	0.65	26.75	63
ASF1030HV	ASF1030HV4R	2.4	0.77	31.6	81
ASF1030HV	ASF1030HV5R	1.6	0.52	33.4	72.75

ID	TASRID	T depth cm	T depth %	Rectal Pressure Before	Ave Anal Pressure Before
ASF1030HV	ASF1030HV6R	2.1	0.68	33.2	65.25
ASF1030HV	ASF1030HV7R	2.7	0.87	28.2	55.5
ASF1030HV	ASF1030HV8R	2.4	0.77	28.6	77.25
ASF1030HV	ASF1030HV9R	1.7	0.55	31.8	64.75
ASF1030HV	ASF1030HV10R	2.2	0.71	24.8	68.75
ASF1030HV	ASF1030HV11R	2.4	0.77	27.8	79.5
ASF1030HV	ASF1030HV12O	1.5	0.48	28.6	63.25
ASF1030HV	ASF1030HV13O	2.8	0.90	31.4	85
ASF1030HV	ASF1030HV14O	2.1	0.68	27.16666667	68.75
ASF1030HV	ASF1030HV15O	2.1	0.68	28.5	72.66666667
ASF1030HV	ASF1030HV16O	1.9	0.61	30.33333333	70.66666667
ASF1030HV	ASF1030HV17O	2	0.65	30.8	90
ASF1030HV	ASF1030HV18O	1.8	0.58	31	100
ASF1030HV	ASF1030HV19O	2	0.65	34.2	79.33333333
ASF1030HV	ASF1030HV20O	2	0.65	28.2	60
ASF1030HV	ASF1030HV21O	3.1	1.00	28.4	73.33333333
ASF1030HV	ASF1030HV22O	1.8	0.58	30	89.66666667
ASF1030HV	ASF1030HV23O	3.1	1.00	33.6	98
ASF1030HV	ASF1030HV24O	1.8	0.58	29.2	91
ASF1030HV	ASF1030HV25O	3.1	1.00	28.6	81.66666667
ASF1031HV	ASF1031HV1R	1	0.26	22	63.75
ASF1031HV	ASF1031HV2R	2	0.51	24	81.66666667
ASF1031HV	ASF1031HV3O	1.3	0.33	27.75	78.5
ASF1031HV	ASF1031HV4O	2	0.51	27.75	66.25
ASF1031HV	ASF1031HV5O	2	0.51	23.25	66.25
ASF1032HV	ASF1032HV1R	1.2	0.32	24.6	76.66666667
ASF1032HV	ASF1032HV2R	1.5	0.41	25	89.33333333
ASF1032HV	ASF1032HV3R	1.4	0.38	23.2	72.75
ASF1032HV	ASF1032HV4O	1.2	0.32	23.2	92.75
ASF1032HV	ASF1032HV5O	1.2	0.32	23.5	72.75
ASF1032HV	ASF1032HV6O	1.9	0.51	23.75	66.5
ASF1032HV	ASF1032HV7O	1.4	0.38	30.5	83.5
ASF1032HV	ASF1032HV8O	1.9	0.51	28.75	77.75
ASF1032HV	ASF1032HV9O	2.1	0.57	30.75	63.75
ASF1032HV	ASF1032HV10O	2.4	0.65	22.25	64.25
ASF1032HV	ASF1032HV11O	2.6	0.70	28.25	54
ASF1033HV	ASF1033HV1R	2.2	0.61	29.2	86.6
ASF1033HV	ASF1033HV2R	1.8	0.50	30.25	81.6
ASF1033HV	ASF1033HV3R	1.3	0.36	36	83.75
ASF1033HV	ASF1033HV4R	1.3	0.36	30.6	87.75
ASF1033HV	ASF1033HV5O	1.7	0.47	38.6	99.5
ASF1033HV	ASF1033HV6O	1.4	0.39	34.4	93.75
ASF1037HV	ASF1037HV1O	1	0.32	27.75	66.75
ASF1037HV	ASF1037HV2R	1.3	0.36	27	68
ASF1037HV	ASF1037HV3R	1.7	0.47	23	74.25

ID	TASRID	T depth cm	T depth %	Rectal Pressure Before	Ave Anal Pressure Before
ASF1008HV	ASF1008HV1R	1.5	0.38	20.4	91
ASF1008HV	ASF1008HV2R	1.8	0.46	21.75	67.75
ASF1008HV	ASF1008HV3R	1.3	0.33	22.2	81
ASF1008HV	ASF1008HV4R	1.1	0.28	21.6	83
ASF1008HV	ASF1008HV5R	1.6	0.41	34.75	73.75
ASF1008HV	ASF1008HV6R	1.7	0.44	25.25	72.25
ASF1008HV	ASF1008HV7R	1.1	0.28	27	73.75
ASF1008HV	ASF1008HV8O	1.3	0.33	30.5	85
ASF1008HV	ASF1008HV9O	1.3	0.33	28.8	79.75
ASF1008HV	ASF1008HV10O	1.1	0.28	28.2	87.75
ASF1008HV	ASF1008HV11O	1.2	0.31	27.2	86
ASF1008HV	ASF1008HV12O	1.2	0.31	30.6	88.75
ASF1008HV	ASF1008HV13O	1.1	0.28	24	87
ASF1008HV	ASF1008HV14O	1.7	0.44	35.4	101.25
ASF1008HV	ASF1008HV15O	2.2	0.56	29.4	93.75
ASF1008HV	ASF1008HV16O	1.4	0.36	24	95.75
ASF1008HV	ASF1008HV17O	1.4	0.36	28.8	109
ASF1008HV	ASF1008HV18O	1.4	0.36	28.4	102.75
ASF1023HV	ASF1023HV1O	1.7	0.38	19.8	82.33333333
ASF1023HV	ASF1023HV2R	1.7	0.38	21.4	80.5
ASF1023HV	ASF1023HV3R	1.7	0.38	21.2	83.66666667
ASF1023HV	ASF1023HV4R	1.7	0.38	20.8	89.33333333
ASF1023HV	ASF1023HV5R	1.7	0.38	20.25	74.5
ASF1023HV	ASF1023HV6R	1	0.22	16.75	86.75
ASF1023HV	ASF1023HV7R	1.7	0.38	16.25	85.5
ASF1023HV	ASF1023HV8R	1.5	0.33	17.5	88.75
ASF1023HV	ASF1023HV9R	1.7	0.38	18.75	77
ASF1023HV	ASF1023HV10R	1.8	0.40	18.5	60.66666667
ASF1002HV	ASF1002HV1R	2.5	0.76	13.67	53.25
ASF1002HV	ASF1002HV2R	3.2	0.97	14.17	53.50
ASF1002HV	ASF1002HV3O	2.1	0.64	11.83	50.75
ASF1002HV	ASF1002HV4O	3.2	0.97	12.33	50.50
ASF1002HV	ASF1002HV5O	2.8	0.85	16.67	44.50
ASF1002HV	ASF1002HV6O	3.3	1.00	15.83	27.00
ASF1002HV	ASF1002HV7O	3.2	0.97	13.50	43.25
ASF1002HV	ASF1002HV8O	3.3	1.00	13.17	44.00
ASF1002HV	ASF1002HV9O	3.1	0.94	14.17	49.50
ASF1002HV	ASF1002HV10O	3.2	0.97	13.33	55.00
ASF1002HV	ASF1002HV11O	3.2	0.97	17.33	53.50
ASF1002HV	ASF1002HV12O	1.6	0.48	14.67	67.75
ASF1002HV	ASF1002HV13O	3.2	0.97	16.17	64.50
ASF1002HV	ASF1002HV14O	1.9	0.58	14.83	57.75
ASF1002HV	ASF1002HV15O	3	0.91	15.33	57.50
ASF1002HV	ASF1002HV16O	1.6	0.48	15.00	63.00
ASF1002HV	ASF1002HV17O	2.3	0.70	19.50	66.25

ID	TASRID	T depth cm	T depth %	Rectal Pressure Before	Ave Anal Pressure Before
ASF1002HV	ASF1002HV18O	2.1	0.64	19.67	70.00
ASF1002HV	ASF1002HV19O	2.4	0.73	17.33	64.75
ASF1002HV	ASF1002HV20O	2.6	0.79	16.17	69.00
ASF1002HV	ASF1002HV21O	3.3	1.00	14.50	70.75
ASF1002HV	ASF1002HV22O	3.3	1.00	15.33	61.25
ASF1002HV	ASF1002HV23O	3.3	1.00	19.50	50.00
ASF1002HV	ASF1002HV24O	3.3	1.00	14.57	55.50
ASF1002HV	ASF1002HV25O	3.3	1.00	16.17	74.00
ASF1002HV	ASF1002HV26O	2.8	0.85	13.50	70.50
ASF1002HV	ASF1002HV27O	3.3	1.00	14.50	50.25
ASF1002HV	ASF1002HV28O	2.3	0.70	13.33	61.75
ASF1002HV	ASF1002HV29O	1.7	0.52	15.67	65.75
ASF1002HV	ASF1002HV30O	3.3	1.00	14.50	68.75
ASF1002HV	ASF1002HV31O	1.2	0.36	14.67	58.75
ASF1002HV	ASF1002HV32O	3.3	1.00	13.33	66.25
ASF1002HV	ASF1002HV33O	3.3	1.00	14.33	62.75
ASF1002HV	ASF1002HV34O	3.3	1.00	16.00	71.00
ASF1002HV	ASF1002HV35O	3.3	1.00	13.83	62.75
ASF1002HV	ASF1002HV36O	1.4	0.42	14.33	71.00
ASF1002HV	ASF1002HV37O	3.3	1.00	15.00	62.25
ASF1002HV	ASF1002HV38O	3.3	1.00	14.50	58.75
ASF1002HV	ASF1002HV39O	3.3	1.00	14.17	66.50
ASF1002HV	ASF1002HV40O	3.3	1.00	18.20	56.25
ASF1002HV	ASF1002HV41O	3.3	1.00	13.50	65.50
ASF1002HV	ASF1002HV42O	3.3	1.00	15.00	55.50
ASF1002HV	ASF1002HV43O	3.3	1.00	16.17	53.25
ASF1002HV	ASF1002HV44O	3.3	1.00	13.50	64.25
ASF1002HV	ASF1002HV43O	2	0.61	14.00	70.25
ASF1002HV	ASF1002HV44O	3.3	1.00	14.67	43.00
ASF1002HV	ASF1002HV45O	3.3	1.00	12.33	64.00
ASF1002HV	ASF1002HV46O	2.4	0.73	13.00	63.75
ASF1002HV	ASF1002HV47O	3.3	1.00	12.67	51.50

ID	TASRID	T Rectal Pressure During	Ave Anal Pressure During	T Anal min pressure
ASF1001HV	ASF1001HV1O	26.40	41.60	26
ASF1001HV	ASF1001HV2O	26.60	52.80	34
ASF1001HV	ASF1001HV3O	28.40	57.80	39
ASF1001HV	ASF1001HV4O	38.20	75.60	47
ASF1001HV	ASF1001HV5O	25.40	0.00	0
ASF1005HV	ASF1005HV1R	15.25	43.50	15
ASF1005HV	ASF1005HV2O	18.50	38.25	18
ASF1007HV	ASF1007HV1O	34.33	27.5	23
ASF1007HV	ASF1007HV2O	40.50	27.50	24
ASF1007HV	ASF1007HV3O	41.20	26.25	17
ASF1007HV	ASF1007HV4O	41.60	35.25	23
ASF1007HV	ASF1007HV5O	31.83	30.00	21
ASF1010HV	ASF1010HV1R	21.75	48.40	24
ASF1010HV	ASF1010HV2O	15.33	50.83	23
ASF1010HV	ASF1010HV3O	13.67	52.83	21
ASF1010HV	ASF1010HV4O	13.33	41.00	22
ASF1010HV	ASF1010HV5O	13.67	49.17	21
ASF1010HV	ASF1010HV6O	14.00	44.17	19
ASF1010HV	ASF1010HV7O	19.33	40.50	25
ASF1011HV	ASF1011HV1R	44.50	64.20	29
ASF1011HV	ASF1011HV2R	56.00	40.75	27
ASF1011HV	ASF1011HV3O	49.25	42.40	24
ASF1012HV	ASF1012HV1R	18.00	39.40	24
ASF1013HV	ASF1013HV1O	23.75	40.80	23
ASF1013HV	ASF1013HV2O	35.40	47.00	31
ASF1013HV	ASF1013HV3O	29.75	50.60	32
ASF1014HV	ASF1014HV1R	15.00	36.60	24
ASF1014HV	ASF1014HV2R	13.00	33.40	17
ASF1014HV	ASF1014HV3R	54.60	66.25	18
ASF1014HV	ASF1014HV4O	57.00	33.80	21
ASF1014HV	ASF1014HV5O	72.50	35.40	26
ASF1014HV	ASF1014HV6O	24.25	30.40	20
ASF1014HV	ASF1014HV7O	63.20	43.20	28
ASF1014HV	ASF1014HV8O	60.75	33.00	22
ASF1014HV	ASF1014HV9O	64.00	36.00	26
ASF1014HV	ASF1014HV10O	58.00	30.80	21
ASF1014HV	ASF1014HV11O	32.75	28.80	22
ASF1014HV	ASF1014HV12O	31.50	29.00	21
ASF1014HV	ASF1014HV13O	76.25	30.25	26
ASF1014HV	ASF1014HV14O	55.00	31.00	26

ID	TASRID	T Rectal Pressure During	Ave Anal Pressure During	T Anal min pressure
ASF1014HV	ASF1014HV15O	17.50	27.75	18
ASF1014HV	ASF1014HV16O	17.25	28.25	19
ASF1014HV	ASF1014HV17O	18.00	24.50	20
ASF1014HV	ASF1014HV18O	18.20	29.00	22
ASF1014HV	ASF1014HV19O	41.40	28.00	22
ASF1014HV	ASF1014HV20O	62.00	31.00	24
ASF1014HV	ASF1014HV21O	32.60	30.50	21
ASF1014HV	ASF1014HV22O	34.00	31.50	23
ASF1014HV	ASF1014HV23O	35.40	30.50	21
ASF1014HV	ASF1014HV24O	53.60	30.75	22
ASF1014HV	ASF1014HV25O	62.40	33.50	24
ASF1017HV	ASF1017HV1R	31.40	48.33	33
ASF1017HV	ASF1017HV2O	23.67	33.00	25
ASF1017HV	ASF1017HV3O	19.17	45.67	26
ASF1017HV	ASF1017HV4O	18.67	38.33	24
ASF1017HV	ASF1017HV5O	22.83	47.67	33
ASF1017HV	ASF1017HV6O	23.83	35.00	29
ASF1017HV	ASF1017HV7O	34.67	41.33	36
ASF1017HV	ASF1017HV8O	21.00	43.00	29
ASF1017HV	ASF1017HV9O	23.00	26.00	25
ASF1017HV	ASF1017HV10O	24.83	40.33	27
ASF1017HV	ASF1017HV11O	28.33	48.33	29
ASF1020HV	ASF1020HV1O	29.00	43.25	29
ASF1020HV	ASF1020HV2O	16.50	41.75	17
ASF1020HV	ASF1020HV3O	18.67	27.25	18
ASF1022HV	ASF1022HV1O	32.17	53.33	34
ASF1025HV	ASF1025HV1O	29.00	51.20	24
ASF1025HV	ASF1025HV2O	26.83	51.80	32
ASF1025HV	ASF1025HV3O	24.20	46.20	22
ASF1025HV	ASF1025HV4O	23.60	38.00	24
ASF1025HV	ASF1025HV5O	20.40	39.20	21
ASF1028HV	ASF1028HV1R	16.5	32.2	24
ASF1028HV	ASF1028HV2O	19	31.8	24
ASF1028HV	ASF1028HV3O	17	34.6	26
ASF1028HV	ASF1028HV4O	24.25	35	25
ASF1028HV	ASF1028HV5O	24.25	38.6	32
ASF1029HV	ASF1029HV1O	19.28571429	25.33333333	13
ASF1029HV	ASF1029HV2O	18.5	26.33333333	16
ASF1029HV	ASF1029HV3O	19.33333333	25.33333333	14
ASF1029HV	ASF1029HV4O	22.33333333	29	15
ASF1030HV	ASF1030HV1R	44.2	39.75	24
ASF1030HV	ASF1030HV2R	38.2	43.25	22
ASF1030HV	ASF1030HV3R	28.25	36.25	21
ASF1030HV	ASF1030HV4R	32.5	33.25	21
ASF1030HV	ASF1030HV5R	39.8	38	21

ID	TASRID	T Rectal Pressure During	Ave Anal Pressure During	T Anal min pressure
ASF1030HV	ASF1030HV6R	35.8	34.25	21
ASF1030HV	ASF1030HV7R	39.2	36.75	21
ASF1030HV	ASF1030HV8R	29.2	32.25	20
ASF1030HV	ASF1030HV9R	29.2	0	0
ASF1030HV	ASF1030HV10R	41.4	30.5	20
ASF1030HV	ASF1030HV11R	38	32.25	21
ASF1030HV	ASF1030HV12O	36.4	41	22
ASF1030HV	ASF1030HV13O	35.16666667	37.33333333	26
ASF1030HV	ASF1030HV14O	34.83333333	40.33333333	26
ASF1030HV	ASF1030HV15O	40.4	40.33333333	28
ASF1030HV	ASF1030HV16O	36.6	36	24
ASF1030HV	ASF1030HV17O	51.2	39	26
ASF1030HV	ASF1030HV18O	55	42	32
ASF1030HV	ASF1030HV19O	40.4	44.66666667	34
ASF1030HV	ASF1030HV20O	50.2	36	29
ASF1030HV	ASF1030HV21O	38	36	27
ASF1030HV	ASF1030HV22O	33.6	43	31
ASF1030HV	ASF1030HV23O	43.8	38.66666667	29
ASF1030HV	ASF1030HV24O	33.4	45.75	32
ASF1030HV	ASF1030HV25O	45.4	37	29
ASF1031HV	ASF1031HV1R	22	57.75	32
ASF1031HV	ASF1031HV2R	25.33333333	39	32
ASF1031HV	ASF1031HV3O	27	43.75	29
ASF1031HV	ASF1031HV4O	26	43.75	30
ASF1031HV	ASF1031HV5O	23.25	36	28
ASF1032HV	ASF1032HV1R	28.4	49.33333333	32
ASF1032HV	ASF1032HV2R	26.4	38	29
ASF1032HV	ASF1032HV3R	24.6	40.25	21
ASF1032HV	ASF1032HV4O	40.4	53.5	29
ASF1032HV	ASF1032HV5O	25.75	54	31
ASF1032HV	ASF1032HV6O	29.25	51.25	26
ASF1032HV	ASF1032HV7O	28.75	54.75	29
ASF1032HV	ASF1032HV8O	28.25	39.75	24
ASF1032HV	ASF1032HV9O	31.4	42	25
ASF1032HV	ASF1032HV10O	43	39	24
ASF1032HV	ASF1032HV11O	34.75	36.75	25
ASF1033HV	ASF1033HV1R	47.4	60.25	49
ASF1033HV	ASF1033HV2R	36	53	38
ASF1033HV	ASF1033HV3R	37.4	64	41
ASF1033HV	ASF1033HV4R	43.4	71.25	45
ASF1033HV	ASF1033HV5O	39.8	72	44
ASF1033HV	ASF1033HV6O	31.2	57	38
ASF1037HV	ASF1037HV1O	26.25	50.25	32
ASF1037HV	ASF1037HV2R	28.75	52.5	31
ASF1037HV	ASF1037HV3R	27	39.75	29

ID	TASRID	T Rectal Pressure During	Ave Anal Pressure During	T Anal min pressure
ASF1008HV	ASF1008HV1R	25.6	65.33333333	23
ASF1008HV	ASF1008HV2R	21.75	41.5	17
ASF1008HV	ASF1008HV3R	20.6	50.33333333	15
ASF1008HV	ASF1008HV4R	20.8	67.75	17
ASF1008HV	ASF1008HV5R	39.25	60.25	22
ASF1008HV	ASF1008HV6R	44.75	59.5	21
ASF1008HV	ASF1008HV7R	27.8	62	21
ASF1008HV	ASF1008HV8O	27.2	67	25
ASF1008HV	ASF1008HV9O	35.2	70.75	28
ASF1008HV	ASF1008HV10O	27.2	64.5	23
ASF1008HV	ASF1008HV11O	27.25	65	23
ASF1008HV	ASF1008HV12O	27.2	64.25	24
ASF1008HV	ASF1008HV13O	24.4	66	20
ASF1008HV	ASF1008HV14O	24.6	76.25	22
ASF1008HV	ASF1008HV15O	41.8	68.5	37
ASF1008HV	ASF1008HV16O	23	80.75	22
ASF1008HV	ASF1008HV17O	33.8	116.25	24
ASF1008HV	ASF1008HV18O	31.4	131.5	27
ASF1023HV	ASF1023HV1O	25.2	58	38
ASF1023HV	ASF1023HV2R	51	26.5	69
ASF1023HV	ASF1023HV3R	60	55.66666667	30
ASF1023HV	ASF1023HV4R	18	40.75	24
ASF1023HV	ASF1023HV5R	20.25	50.5	26
ASF1023HV	ASF1023HV6R	21.5	53	34
ASF1023HV	ASF1023HV7R	25	43.75	27
ASF1023HV	ASF1023HV8R	21	50.75	29
ASF1023HV	ASF1023HV9R	18.75	44.5	27
ASF1023HV	ASF1023HV10R	30.75	57.25	35
ASF1002HV	ASF1002HV1R	15.17	29.00	11
ASF1002HV	ASF1002HV2R	15.00	26.75	16
ASF1002HV	ASF1002HV3O	21.50	29.00	10
ASF1002HV	ASF1002HV4O	12.83	21.75	11
ASF1002HV	ASF1002HV5O	18.50	29.50	17
ASF1002HV	ASF1002HV6O	20.50	20.75	12
ASF1002HV	ASF1002HV7O	16.00	22.50	15
ASF1002HV	ASF1002HV8O	23.67	17.50	13
ASF1002HV	ASF1002HV9O	15.67	21.00	12
ASF1002HV	ASF1002HV10O	17.17	20.75	14
ASF1002HV	ASF1002HV11O	22.33	21.50	13
ASF1002HV	ASF1002HV12O	22.17	37.25	17
ASF1002HV	ASF1002HV13O	18.50	19.00	13
ASF1002HV	ASF1002HV14O	12.83	34.00	13
ASF1002HV	ASF1002HV15O	20.00	26.00	18
ASF1002HV	ASF1002HV16O	16.83	39.00	16
ASF1002HV	ASF1002HV17O	38.33	37.00	20

ID	TASRID	T Rectal Pressure During	Ave Anal Pressure During	T Anal min pressure
ASF1002HV	ASF1002HV18O	23.00	33.00	15
ASF1002HV	ASF1002HV19O	16.50	27.75	14
ASF1002HV	ASF1002HV20O	17.50	27.75	15
ASF1002HV	ASF1002HV21O	22.00	26.00	14
ASF1002HV	ASF1002HV22O	27.50	27.50	19
ASF1002HV	ASF1002HV23O	22.50	22.25	21
ASF1002HV	ASF1002HV24O	24.00	17.50	13
ASF1002HV	ASF1002HV25O	19.17	25.75	15
ASF1002HV	ASF1002HV26O	18.00	26.75	15
ASF1002HV	ASF1002HV27O	19.83	20.50	15
ASF1002HV	ASF1002HV28O	13.67	33.00	13
ASF1002HV	ASF1002HV29O	16.00	51.00	21
ASF1002HV	ASF1002HV30O	17.00	23.25	15
ASF1002HV	ASF1002HV31O	15.33	30.25	16
ASF1002HV	ASF1002HV32O	13.67	25.75	13
ASF1002HV	ASF1002HV33O	24.00	20.25	13
ASF1002HV	ASF1002HV34O	16.33	23.50	15
ASF1002HV	ASF1002HV35O	21.67	22.00	15
ASF1002HV	ASF1002HV36O	16.17	53.50	34
ASF1002HV	ASF1002HV37O	15.50	22.25	14
ASF1002HV	ASF1002HV38O	15.00	21.00	12
ASF1002HV	ASF1002HV39O	17.33	22.75	13
ASF1002HV	ASF1002HV40O	21.67	19.25	14
ASF1002HV	ASF1002HV41O	15.67	27.50	13
ASF1002HV	ASF1002HV42O	16.83	20.50	14
ASF1002HV	ASF1002HV43O	26.00	16.50	13
ASF1002HV	ASF1002HV44O	100.00	27.00	13
ASF1002HV	ASF1002HV43O	13.83	39.00	15
ASF1002HV	ASF1002HV44O	24.83	16.25	13
ASF1002HV	ASF1002HV45O	13.00	25.25	15
ASF1002HV	ASF1002HV46O	12.17	34.00	15
ASF1002HV	ASF1002HV47O	15.50	19.75	11

ID	TASRID	Ave Anal Pressure Change	% anal pressure change
ASF1001HV	ASF1001HV1O	-27.00	-39.36
ASF1001HV	ASF1001HV2O	-12.40	-19.02
ASF1001HV	ASF1001HV3O	-19.00	-24.74
ASF1001HV	ASF1001HV4O	-7.20	-8.70
ASF1001HV	ASF1001HV5O	-79.80	-100.00
ASF1005HV	ASF1005HV1R	-8.50	-16.35
ASF1005HV	ASF1005HV2O	-11.35	-22.88
ASF1007HV	ASF1007HV1O	-20.00	-42.11
ASF1007HV	ASF1007HV2O	-20.75	-43.01
ASF1007HV	ASF1007HV3O	-36.25	-58.00
ASF1007HV	ASF1007HV4O	-27.75	-44.05
ASF1007HV	ASF1007HV5O	-31.75	-51.42
ASF1010HV	ASF1010HV1R	-60.60	-55.60
ASF1010HV	ASF1010HV2O	-31.67	-38.38
ASF1010HV	ASF1010HV3O	-37.67	-41.62
ASF1010HV	ASF1010HV4O	-52.00	-55.91
ASF1010HV	ASF1010HV5O	-39.83	-44.76
ASF1010HV	ASF1010HV6O	-22.50	-33.75
ASF1010HV	ASF1010HV7O	-31.00	-43.36
ASF1011HV	ASF1011HV1R	-35.60	-35.67
ASF1011HV	ASF1011HV2R	-70.05	-63.22
ASF1011HV	ASF1011HV3O	-46.40	-52.25
ASF1012HV	ASF1012HV1R	-36.00	-47.75
ASF1013HV	ASF1013HV1O	-22.40	-35.44
ASF1013HV	ASF1013HV2O	-21.60	-31.49
ASF1013HV	ASF1013HV3O	-16.00	-24.02
ASF1014HV	ASF1014HV1R	-15.80	-30.15
ASF1014HV	ASF1014HV2R	-23.10	-40.88
ASF1014HV	ASF1014HV3R	11.25	20.45
ASF1014HV	ASF1014HV4O	-12.70	-27.31
ASF1014HV	ASF1014HV5O	-16.20	-31.40
ASF1014HV	ASF1014HV6O	-1.60	-5.00
ASF1014HV	ASF1014HV7O	-2.20	-4.85
ASF1014HV	ASF1014HV8O	-12.60	-27.63
ASF1014HV	ASF1014HV9O	-18.80	-34.31
ASF1014HV	ASF1014HV10O	-23.40	-43.17
ASF1014HV	ASF1014HV11O	-11.20	-28.00
ASF1014HV	ASF1014HV12O	-9.40	-24.48
ASF1014HV	ASF1014HV13O	-19.55	-39.26
ASF1014HV	ASF1014HV14O	-31.00	-50.00

ID	TASRID	Ave Anal Pressure Change	% anal pressure change
ASF1014HV	ASF1014HV15O	-20.75	-42.78
ASF1014HV	ASF1014HV16O	-16.25	-36.52
ASF1014HV	ASF1014HV17O	-14.25	-36.77
ASF1014HV	ASF1014HV18O	-15.67	-35.07
ASF1014HV	ASF1014HV19O	-21.00	-42.86
ASF1014HV	ASF1014HV20O	-15.25	-32.97
ASF1014HV	ASF1014HV21O	-18.75	-38.07
ASF1014HV	ASF1014HV22O	-20.00	-38.83
ASF1014HV	ASF1014HV23O	-13.00	-29.89
ASF1014HV	ASF1014HV24O	-16.50	-34.92
ASF1014HV	ASF1014HV25O	-14.75	-30.57
ASF1017HV	ASF1017HV1R	-12.67	-20.77
ASF1017HV	ASF1017HV2O	-24.00	-42.11
ASF1017HV	ASF1017HV3O	-19.00	-29.38
ASF1017HV	ASF1017HV4O	-27.00	-41.33
ASF1017HV	ASF1017HV5O	-23.33	-32.86
ASF1017HV	ASF1017HV6O	-30.00	-46.15
ASF1017HV	ASF1017HV7O	-26.00	-38.61
ASF1017HV	ASF1017HV8O	-32.00	-42.67
ASF1017HV	ASF1017HV9O	-27.00	-50.94
ASF1017HV	ASF1017HV10O	-23.17	-36.48
ASF1017HV	ASF1017HV11O	-21.33	-30.62
ASF1020HV	ASF1020HV1O	3.50	8.81
ASF1020HV	ASF1020HV2O	-31.50	-43.00
ASF1020HV	ASF1020HV3O	-40.25	-59.63
ASF1022HV	ASF1022HV1O	-38.33	-41.82
ASF1025HV	ASF1025HV1O	-25.60	-33.33
ASF1025HV	ASF1025HV2O	-23.00	-30.75
ASF1025HV	ASF1025HV3O	-20.00	-30.21
ASF1025HV	ASF1025HV4O	-16.40	-30.15
ASF1025HV	ASF1025HV5O	-17.40	-30.74
ASF1028HV	ASF1028HV1R	-6.60	-17.01
ASF1028HV	ASF1028HV2O	-21.20	-40.00
ASF1028HV	ASF1028HV3O	-19.00	-35.45
ASF1028HV	ASF1028HV4O	-15.80	-31.10
ASF1028HV	ASF1028HV5O	-13.60	-26.05
ASF1029HV	ASF1029HV1O	-23.33	-47.95
ASF1029HV	ASF1029HV2O	-19.67	-42.75
ASF1029HV	ASF1029HV3O	-11.33	-30.91
ASF1029HV	ASF1029HV4O	-14.33	-33.08
ASF1030HV	ASF1030HV1R	-26.50	-40.00
ASF1030HV	ASF1030HV2R	-29.50	-40.55
ASF1030HV	ASF1030HV3R	-26.75	-42.46
ASF1030HV	ASF1030HV4R	-47.75	-58.95
ASF1030HV	ASF1030HV5R	-34.75	-47.77

ID	TASRID	Ave Anal Pressure Change	% anal pressure change
ASF1030HV	ASF1030HV6R	-31.00	-47.51
ASF1030HV	ASF1030HV7R	-18.75	-33.78
ASF1030HV	ASF1030HV8R	-45.00	-58.25
ASF1030HV	ASF1030HV9R	-64.75	-100.00
ASF1030HV	ASF1030HV10R	-38.25	-55.64
ASF1030HV	ASF1030HV11R	-47.25	-59.43
ASF1030HV	ASF1030HV12O	-22.25	-35.18
ASF1030HV	ASF1030HV13O	-47.67	-56.08
ASF1030HV	ASF1030HV14O	-28.42	-41.33
ASF1030HV	ASF1030HV15O	-32.33	-44.50
ASF1030HV	ASF1030HV16O	-34.67	-49.06
ASF1030HV	ASF1030HV17O	-51.00	-56.67
ASF1030HV	ASF1030HV18O	-58.00	-58.00
ASF1030HV	ASF1030HV19O	-34.67	-43.70
ASF1030HV	ASF1030HV20O	-24.00	-40.00
ASF1030HV	ASF1030HV21O	-37.33	-50.91
ASF1030HV	ASF1030HV22O	-46.67	-52.04
ASF1030HV	ASF1030HV23O	-59.33	-60.54
ASF1030HV	ASF1030HV24O	-45.25	-49.73
ASF1030HV	ASF1030HV25O	-44.67	-54.69
ASF1031HV	ASF1031HV1R	-6.00	-9.41
ASF1031HV	ASF1031HV2R	-42.67	-52.24
ASF1031HV	ASF1031HV3O	-34.75	-44.27
ASF1031HV	ASF1031HV4O	-22.50	-33.96
ASF1031HV	ASF1031HV5O	-30.25	-45.66
ASF1032HV	ASF1032HV1R	-27.33	-35.65
ASF1032HV	ASF1032HV2R	-51.33	-57.46
ASF1032HV	ASF1032HV3R	-32.50	-44.67
ASF1032HV	ASF1032HV4O	-39.25	-42.32
ASF1032HV	ASF1032HV5O	-18.75	-25.77
ASF1032HV	ASF1032HV6O	-15.25	-22.93
ASF1032HV	ASF1032HV7O	-28.75	-34.43
ASF1032HV	ASF1032HV8O	-38.00	-48.87
ASF1032HV	ASF1032HV9O	-21.75	-34.12
ASF1032HV	ASF1032HV10O	-25.25	-39.30
ASF1032HV	ASF1032HV11O	-17.25	-31.94
ASF1033HV	ASF1033HV1R	-26.35	-30.43
ASF1033HV	ASF1033HV2R	-28.60	-35.05
ASF1033HV	ASF1033HV3R	-19.75	-23.58
ASF1033HV	ASF1033HV4R	-16.50	-18.80
ASF1033HV	ASF1033HV5O	-27.50	-27.64
ASF1033HV	ASF1033HV6O	-36.75	-39.20
ASF1037HV	ASF1037HV1O	-16.50	-24.72
ASF1037HV	ASF1037HV2R	-15.50	-22.79
ASF1037HV	ASF1037HV3R	-34.50	-46.46

ID	TASRID	Ave Anal Pressure Change	% anal pressure change
ASF1008HV	ASF1008HV1R	-25.67	-28.21
ASF1008HV	ASF1008HV2R	-26.25	-38.75
ASF1008HV	ASF1008HV3R	-30.67	-37.86
ASF1008HV	ASF1008HV4R	-15.25	-18.37
ASF1008HV	ASF1008HV5R	-13.50	-18.31
ASF1008HV	ASF1008HV6R	-12.75	-17.65
ASF1008HV	ASF1008HV7R	-11.75	0.00
ASF1008HV	ASF1008HV8O	-18.00	-21.18
ASF1008HV	ASF1008HV9O	-9.00	-11.29
ASF1008HV	ASF1008HV10O	-23.25	-26.50
ASF1008HV	ASF1008HV11O	-21.00	-24.42
ASF1008HV	ASF1008HV12O	-24.50	-27.61
ASF1008HV	ASF1008HV13O	-21.00	-24.14
ASF1008HV	ASF1008HV14O	-25.00	-24.69
ASF1008HV	ASF1008HV15O	-25.25	-26.93
ASF1008HV	ASF1008HV16O	-15.00	-15.67
ASF1008HV	ASF1008HV17O	7.25	6.65
ASF1008HV	ASF1008HV18O	28.75	27.98
ASF1023HV	ASF1023HV1O	-24.33	-29.55
ASF1023HV	ASF1023HV2R	-54.00	-67.08
ASF1023HV	ASF1023HV3R	-28.00	-33.47
ASF1023HV	ASF1023HV4R	-48.58	-54.38
ASF1023HV	ASF1023HV5R	-24.00	-32.21
ASF1023HV	ASF1023HV6R	-33.75	-38.90
ASF1023HV	ASF1023HV7R	-41.75	-48.83
ASF1023HV	ASF1023HV8R	-38.00	-42.82
ASF1023HV	ASF1023HV9R	-32.50	-42.21
ASF1023HV	ASF1023HV10R	-3.42	-5.63
ASF1002HV	ASF1002HV1R	-24.25	-45.54
ASF1002HV	ASF1002HV2R	-26.75	-50.00
ASF1002HV	ASF1002HV3O	-21.75	-42.86
ASF1002HV	ASF1002HV4O	-28.75	-56.93
ASF1002HV	ASF1002HV5O	-15.00	-33.71
ASF1002HV	ASF1002HV6O	-6.25	-23.15
ASF1002HV	ASF1002HV7O	-20.75	-47.98
ASF1002HV	ASF1002HV8O	-26.50	-60.23
ASF1002HV	ASF1002HV9O	-28.50	-57.58
ASF1002HV	ASF1002HV10O	-34.25	-62.27
ASF1002HV	ASF1002HV11O	-32.00	-59.81
ASF1002HV	ASF1002HV12O	-30.50	-45.02
ASF1002HV	ASF1002HV13O	-45.50	-70.54
ASF1002HV	ASF1002HV14O	-23.75	-41.13
ASF1002HV	ASF1002HV15O	-31.50	-54.78
ASF1002HV	ASF1002HV16O	-24.00	-38.10
ASF1002HV	ASF1002HV17O	-29.25	-44.15

ID	TASRID	Ave Anal Pressure Change	% anal pressure change
ASF1002HV	ASF1002HV18O	-37.00	-52.86
ASF1002HV	ASF1002HV19O	-37.00	-57.14
ASF1002HV	ASF1002HV20O	-41.25	-59.78
ASF1002HV	ASF1002HV21O	-44.75	-63.25
ASF1002HV	ASF1002HV22O	-33.75	-55.10
ASF1002HV	ASF1002HV23O	-27.75	-55.50
ASF1002HV	ASF1002HV24O	-38.00	-68.47
ASF1002HV	ASF1002HV25O	-48.25	-65.20
ASF1002HV	ASF1002HV26O	-43.75	-62.06
ASF1002HV	ASF1002HV27O	-29.75	-59.20
ASF1002HV	ASF1002HV28O	-28.75	-46.56
ASF1002HV	ASF1002HV29O	-14.75	-22.43
ASF1002HV	ASF1002HV30O	-45.50	-66.18
ASF1002HV	ASF1002HV31O	-28.50	-48.51
ASF1002HV	ASF1002HV32O	-40.50	-61.13
ASF1002HV	ASF1002HV33O	-42.50	-67.73
ASF1002HV	ASF1002HV34O	-47.50	-66.90
ASF1002HV	ASF1002HV35O	-40.75	-64.94
ASF1002HV	ASF1002HV36O	-17.50	-24.65
ASF1002HV	ASF1002HV37O	-40.00	-64.26
ASF1002HV	ASF1002HV38O	-37.75	-64.26
ASF1002HV	ASF1002HV39O	-43.75	-65.79
ASF1002HV	ASF1002HV40O	-37.00	-65.78
ASF1002HV	ASF1002HV41O	-38.00	-58.02
ASF1002HV	ASF1002HV42O	-35.00	-63.06
ASF1002HV	ASF1002HV43O	-36.75	-69.01
ASF1002HV	ASF1002HV44O	-37.25	-57.98
ASF1002HV	ASF1002HV43O	-31.25	-44.48
ASF1002HV	ASF1002HV44O	-26.75	-62.21
ASF1002HV	ASF1002HV45O	-38.75	-60.55
ASF1002HV	ASF1002HV46O	-29.75	-46.67
ASF1002HV	ASF1002HV47O	-31.75	-61.65

ID	TASRID	Ave rectal pressure change	% rectal pressure change	passed wind
ASF1001HV	ASF1001HV1O	0.80	3.12	0
ASF1001HV	ASF1001HV2O	-0.80	-2.92	0
ASF1001HV	ASF1001HV3O	3.40	13.60	0
ASF1001HV	ASF1001HV4O	10.40	37.41	0
ASF1001HV	ASF1001HV5O	-2.80	-9.93	0
ASF1005HV	ASF1005HV1R	3.00	24.49	0
ASF1005HV	ASF1005HV2O	2.50	15.63	0
ASF1007HV	ASF1007HV1O	-2.83	-7.62	0
ASF1007HV	ASF1007HV2O	-2.30	-5.37	1
ASF1007HV	ASF1007HV3O	9.53	30.11	1
ASF1007HV	ASF1007HV4O	4.80	13.04	0
ASF1007HV	ASF1007HV5O	-5.00	-13.57	0
ASF1010HV	ASF1010HV1R	4.25	24.29	0
ASF1010HV	ASF1010HV2O	1.33	9.52	0
ASF1010HV	ASF1010HV3O	4.00	41.38	0
ASF1010HV	ASF1010HV4O	3.33	33.33	0
ASF1010HV	ASF1010HV5O	-1.33	-8.89	0
ASF1010HV	ASF1010HV6O	4.00	40.00	0
ASF1010HV	ASF1010HV7O	6.33	48.72	0
ASF1011HV	ASF1011HV1R	1.25	2.89	0
ASF1011HV	ASF1011HV2R	6.33	12.75	0
ASF1011HV	ASF1011HV3O	10.00	25.48	0
ASF1012HV	ASF1012HV1R	0.60	3.45	0
ASF1013HV	ASF1013HV1O	-5.25	-18.10	0
ASF1013HV	ASF1013HV2O	5.15	17.02	0
ASF1013HV	ASF1013HV3O	8.75	41.67	0
ASF1014HV	ASF1014HV1R	1.75	13.21	0
ASF1014HV	ASF1014HV2R	-4.25	-24.64	0
ASF1014HV	ASF1014HV3R	42.00	333.33	0
ASF1014HV	ASF1014HV4O	42.25	286.44	0
ASF1014HV	ASF1014HV5O	52.50	262.50	0
ASF1014HV	ASF1014HV6O	7.00	40.58	0
ASF1014HV	ASF1014HV7O	45.45	256.06	0
ASF1014HV	ASF1014HV8O	43.50	252.17	0
ASF1014HV	ASF1014HV9O	41.00	178.26	0
ASF1014HV	ASF1014HV10O	39.50	213.51	0
ASF1014HV	ASF1014HV11O	14.00	74.67	0
ASF1014HV	ASF1014HV12O	14.25	82.61	0
ASF1014HV	ASF1014HV13O	56.00	276.54	0
ASF1014HV	ASF1014HV14O	31.75	136.56	0

ID	TASRID	Ave rectal pressure change	% rectal pressure change	passed wind
ASF1014HV	ASF1014HV15O	-5.25	-23.08	0
ASF1014HV	ASF1014HV16O	-1.00	-5.48	0
ASF1014HV	ASF1014HV17O	0.50	2.86	0
ASF1014HV	ASF1014HV18O	0.00	0.00	0
ASF1014HV	ASF1014HV19O	22.40	117.89	0
ASF1014HV	ASF1014HV20O	42.60	219.59	0
ASF1014HV	ASF1014HV21O	15.20	87.36	0
ASF1014HV	ASF1014HV22O	2.60	8.28	0
ASF1014HV	ASF1014HV23O	11.20	46.28	0
ASF1014HV	ASF1014HV24O	29.00	117.89	0
ASF1014HV	ASF1014HV25O	38.40	160.00	0
ASF1017HV	ASF1017HV1R	6.80	27.64	0
ASF1017HV	ASF1017HV2O	1.27	5.65	0
ASF1017HV	ASF1017HV3O	-3.67	-16.06	0
ASF1017HV	ASF1017HV4O	-3.18	-14.56	0
ASF1017HV	ASF1017HV5O	-0.17	-0.72	0
ASF1017HV	ASF1017HV6O	2.33	10.85	1
ASF1017HV	ASF1017HV7O	7.50	27.61	0
ASF1017HV	ASF1017HV8O	-4.83	-18.71	0
ASF1017HV	ASF1017HV9O	5.00	27.78	0
ASF1017HV	ASF1017HV10O	-1.33	-5.10	0
ASF1017HV	ASF1017HV11O	2.67	10.39	0
ASF1020HV	ASF1020HV1O	15.17	109.64	0
ASF1020HV	ASF1020HV2O	-1.33	-7.48	0
ASF1020HV	ASF1020HV3O	0.67	3.70	0
ASF1022HV	ASF1022HV1O	0.83	2.66	0
ASF1025HV	ASF1025HV1O	4.80	19.83	0
ASF1025HV	ASF1025HV2O	1.23	4.82	0
ASF1025HV	ASF1025HV3O	2.20	10.00	0
ASF1025HV	ASF1025HV4O	2.80	13.46	0
ASF1025HV	ASF1025HV5O	0.20	0.99	0
ASF1028HV	ASF1028HV1R	-4.25	-20.48	0
ASF1028HV	ASF1028HV2O	-10.50	-35.59	0
ASF1028HV	ASF1028HV3O	-13.00	-43.33	0
ASF1028HV	ASF1028HV4O	-4.00	-14.16	0
ASF1028HV	ASF1028HV5O	-8.00	-24.81	0
ASF1029HV	ASF1029HV1O	-2.14	-10.00	0
ASF1029HV	ASF1029HV2O	0.00	0.00	0
ASF1029HV	ASF1029HV3O	1.00	5.45	0
ASF1029HV	ASF1029HV4O	-0.83	-3.60	0
ASF1030HV	ASF1030HV1R	13.87	45.71	0
ASF1030HV	ASF1030HV2R	-4.20	-9.91	0
ASF1030HV	ASF1030HV3R	1.50	5.61	0
ASF1030HV	ASF1030HV4R	0.90	2.85	0
ASF1030HV	ASF1030HV5R	6.40	19.16	0

ID	TASRID	Ave rectal pressure change	% rectal pressure change	passed wind
ASF1030HV	ASF1030HV6R	2.60	7.83	0
ASF1030HV	ASF1030HV7R	11.00	39.01	0
ASF1030HV	ASF1030HV8R	0.60	2.10	0
ASF1030HV	ASF1030HV9R	-2.60	-8.18	0
ASF1030HV	ASF1030HV10R	16.60	66.94	0
ASF1030HV	ASF1030HV11R	10.20	36.69	0
ASF1030HV	ASF1030HV12O	7.80	27.27	0
ASF1030HV	ASF1030HV13O	3.77	12.00	0
ASF1030HV	ASF1030HV14O	7.67	28.22	0
ASF1030HV	ASF1030HV15O	11.90	41.75	0
ASF1030HV	ASF1030HV16O	6.27	20.66	0
ASF1030HV	ASF1030HV17O	20.40	66.23	0
ASF1030HV	ASF1030HV18O	24.00	77.42	0
ASF1030HV	ASF1030HV19O	6.20	18.13	0
ASF1030HV	ASF1030HV20O	22.00	78.01	0
ASF1030HV	ASF1030HV21O	9.60	33.80	0
ASF1030HV	ASF1030HV22O	3.60	12.00	0
ASF1030HV	ASF1030HV23O	10.20	30.36	0
ASF1030HV	ASF1030HV24O	4.20	14.38	0
ASF1030HV	ASF1030HV25O	16.80	58.74	0
ASF1031HV	ASF1031HV1R	0.00	0.00	0
ASF1031HV	ASF1031HV2R	1.33	5.56	0
ASF1031HV	ASF1031HV3O	-0.75	-2.70	0
ASF1031HV	ASF1031HV4O	-1.75	-6.31	0
ASF1031HV	ASF1031HV5O	0.00	0.00	0
ASF1032HV	ASF1032HV1R	3.80	15.45	0
ASF1032HV	ASF1032HV2R	1.40	5.60	0
ASF1032HV	ASF1032HV3R	1.40	6.03	0
ASF1032HV	ASF1032HV4O	17.20	74.14	0
ASF1032HV	ASF1032HV5O	2.25	9.57	0
ASF1032HV	ASF1032HV6O	5.50	23.16	0
ASF1032HV	ASF1032HV7O	-1.75	-5.74	0
ASF1032HV	ASF1032HV8O	-0.50	-1.74	0
ASF1032HV	ASF1032HV9O	0.65	2.11	0
ASF1032HV	ASF1032HV10O	20.75	93.26	0
ASF1032HV	ASF1032HV11O	6.50	23.01	0
ASF1033HV	ASF1033HV1R	18.20	62.33	0
ASF1033HV	ASF1033HV2R	5.75	19.01	0
ASF1033HV	ASF1033HV3R	1.40	3.89	0
ASF1033HV	ASF1033HV4R	12.80	41.83	0
ASF1033HV	ASF1033HV5O	1.20	3.11	0
ASF1033HV	ASF1033HV6O	-3.20	-9.30	0
ASF1037HV	ASF1037HV1O	-1.50	-5.41	0
ASF1037HV	ASF1037HV2R	1.75	6.48	0
ASF1037HV	ASF1037HV3R	4.00	17.39	0

ID	TASRID	Ave rectal pressure change	% rectal pressure change	passed wind
ASF1008HV	ASF1008HV1R	5.20	25.49	0
ASF1008HV	ASF1008HV2R	0.00	0.00	0
ASF1008HV	ASF1008HV3R	-1.60	-7.21	0
ASF1008HV	ASF1008HV4R	-0.80	-3.70	0
ASF1008HV	ASF1008HV5R	4.50	12.95	0
ASF1008HV	ASF1008HV6R	19.50	77.23	0
ASF1008HV	ASF1008HV7R	0.00	0.00	0
ASF1008HV	ASF1008HV8O	-3.30	-10.82	0
ASF1008HV	ASF1008HV9O	6.40	22.22	0
ASF1008HV	ASF1008HV10O	-1.00	-3.55	0
ASF1008HV	ASF1008HV11O	0.05	0.18	0
ASF1008HV	ASF1008HV12O	-3.40	-11.11	0
ASF1008HV	ASF1008HV13O	0.40	1.67	0
ASF1008HV	ASF1008HV14O	-10.80	-30.51	1
ASF1008HV	ASF1008HV15O	12.40	42.18	0
ASF1008HV	ASF1008HV16O	-1.00	-4.17	0
ASF1008HV	ASF1008HV17O	5.00	17.36	0
ASF1008HV	ASF1008HV18O	3.00	10.56	0
ASF1023HV	ASF1023HV1O	5.40	27.27	0
ASF1023HV	ASF1023HV2R	29.60	138.32	0
ASF1023HV	ASF1023HV3R	38.80	183.02	0
ASF1023HV	ASF1023HV4R	-2.80	-13.46	0
ASF1023HV	ASF1023HV5R	0.00	0.00	0
ASF1023HV	ASF1023HV6R	4.75	28.36	0
ASF1023HV	ASF1023HV7R	8.75	53.85	0
ASF1023HV	ASF1023HV8R	3.50	20.00	0
ASF1023HV	ASF1023HV9R	0.00	0.00	0
ASF1023HV	ASF1023HV10R	12.25	66.22	0
ASF1002HV	ASF1002HV1R	1.50	10.98	0
ASF1002HV	ASF1002HV2R	0.83	5.88	0
ASF1002HV	ASF1002HV3O	9.67	81.69	0
ASF1002HV	ASF1002HV4O	0.50	4.05	0
ASF1002HV	ASF1002HV5O	1.83	11.00	0
ASF1002HV	ASF1002HV6O	4.67	29.47	0
ASF1002HV	ASF1002HV7O	2.50	18.52	0
ASF1002HV	ASF1002HV8O	10.50	79.75	1
ASF1002HV	ASF1002HV9O	1.50	10.59	0
ASF1002HV	ASF1002HV10O	3.83	28.75	1
ASF1002HV	ASF1002HV11O	5.00	28.85	1
ASF1002HV	ASF1002HV12O	7.50	51.14	0
ASF1002HV	ASF1002HV13O	2.33	14.43	1
ASF1002HV	ASF1002HV14O	-2.00	-13.48	0
ASF1002HV	ASF1002HV15O	4.67	30.43	0
ASF1002HV	ASF1002HV16O	1.83	12.22	0
ASF1002HV	ASF1002HV17O	18.83	96.58	1

ID	TASRID	Ave rectal pressure change	% rectal pressure change	passed wind
ASF1002HV	ASF1002HV18O	3.33	16.95	0
ASF1002HV	ASF1002HV19O	-0.83	-4.81	0
ASF1002HV	ASF1002HV20O	1.33	8.25	0
ASF1002HV	ASF1002HV21O	7.50	51.72	0
ASF1002HV	ASF1002HV22O	12.17	79.35	1
ASF1002HV	ASF1002HV23O	3.00	15.38	1
ASF1002HV	ASF1002HV24O	9.43	64.71	1
ASF1002HV	ASF1002HV25O	3.00	18.56	1
ASF1002HV	ASF1002HV26O	4.50	33.33	0
ASF1002HV	ASF1002HV27O	5.33	36.78	1
ASF1002HV	ASF1002HV28O	0.33	2.50	0
ASF1002HV	ASF1002HV29O	0.33	2.13	0
ASF1002HV	ASF1002HV30O	2.50	17.24	0
ASF1002HV	ASF1002HV31O	0.67	4.55	0
ASF1002HV	ASF1002HV32O	0.33	2.50	0
ASF1002HV	ASF1002HV33O	9.67	67.44	1
ASF1002HV	ASF1002HV34O	0.33	2.08	1
ASF1002HV	ASF1002HV35O	7.83	56.63	1
ASF1002HV	ASF1002HV36O	1.83	12.79	0
ASF1002HV	ASF1002HV37O	0.50	3.33	0
ASF1002HV	ASF1002HV38O	0.50	3.45	0
ASF1002HV	ASF1002HV39O	3.17	22.35	0
ASF1002HV	ASF1002HV40O	3.47	19.05	1
ASF1002HV	ASF1002HV41O	2.17	16.05	0
ASF1002HV	ASF1002HV42O	1.83	12.22	0
ASF1002HV	ASF1002HV43O	9.83	60.82	1
ASF1002HV	ASF1002HV44O	86.50	640.74	0
ASF1002HV	ASF1002HV43O	-0.17	-1.19	0
ASF1002HV	ASF1002HV44O	10.17	69.32	1
ASF1002HV	ASF1002HV45O	0.67	5.41	0
ASF1002HV	ASF1002HV46O	-0.83	-6.41	0
ASF1002HV	ASF1002HV47O	2.83	22.37	0

ID	TASRID	passed stool	burped
ASF1001HV	ASF1001HV1O	0	0
ASF1001HV	ASF1001HV2O	0	0
ASF1001HV	ASF1001HV3O	0	0
ASF1001HV	ASF1001HV4O	0	0
ASF1001HV	ASF1001HV5O	0	0
ASF1005HV	ASF1005HV1R	0	0
ASF1005HV	ASF1005HV2O	0	0
ASF1007HV	ASF1007HV1O	0	0
ASF1007HV	ASF1007HV2O	0	0
ASF1007HV	ASF1007HV3O	0	0
ASF1007HV	ASF1007HV4O	0	0
ASF1007HV	ASF1007HV5O	0	0
ASF1010HV	ASF1010HV1R	0	0
ASF1010HV	ASF1010HV2O	0	0
ASF1010HV	ASF1010HV3O	0	0
ASF1010HV	ASF1010HV4O	0	0
ASF1010HV	ASF1010HV5O	0	0
ASF1010HV	ASF1010HV6O	0	0
ASF1010HV	ASF1010HV7O	0	0
ASF1011HV	ASF1011HV1R	0	0
ASF1011HV	ASF1011HV2R	0	0
ASF1011HV	ASF1011HV3O	0	0
ASF1012HV	ASF1012HV1R	0	0
ASF1013HV	ASF1013HV1O	0	0
ASF1013HV	ASF1013HV2O	0	0
ASF1013HV	ASF1013HV3O	0	0
ASF1014HV	ASF1014HV1R	0	0
ASF1014HV	ASF1014HV2R	0	0
ASF1014HV	ASF1014HV3R	0	0
ASF1014HV	ASF1014HV4O	0	0
ASF1014HV	ASF1014HV5O	0	0
ASF1014HV	ASF1014HV6O	0	0
ASF1014HV	ASF1014HV7O	0	0
ASF1014HV	ASF1014HV8O	0	0
ASF1014HV	ASF1014HV9O	0	0
ASF1014HV	ASF1014HV10O	0	0
ASF1014HV	ASF1014HV11O	0	0
ASF1014HV	ASF1014HV12O	0	0
ASF1014HV	ASF1014HV13O	0	0
ASF1014HV	ASF1014HV14O	0	0

TASRID
AC length
R resting time
O resting time
TASR
T pre/post meal
T time
T Occurance
T perception
T perception type
T score
T duration
T depth cm
T depth %
Rectal Pressure Before
Ave Anal Pressure Before
T Rectal Pressure During
Ave Anal Pressure During
T Anal min pressure
Ave Anal Pressure Change
% anal pressure change
Ave rectal pressure change
% rectal pressure change
passed wind
passed stool

ID	TASRID	passed stool	burped
ASF1014HV	ASF1014HV15O	0	0
ASF1014HV	ASF1014HV16O	0	0
ASF1014HV	ASF1014HV17O	0	0
ASF1014HV	ASF1014HV18O	0	0
ASF1014HV	ASF1014HV19O	0	0
ASF1014HV	ASF1014HV20O	0	0
ASF1014HV	ASF1014HV21O	0	0
ASF1014HV	ASF1014HV22O	0	0
ASF1014HV	ASF1014HV23O	0	0
ASF1014HV	ASF1014HV24O	0	0
ASF1014HV	ASF1014HV25O	0	0
ASF1017HV	ASF1017HV1R	0	0
ASF1017HV	ASF1017HV2O	0	0
ASF1017HV	ASF1017HV3O	0	0
ASF1017HV	ASF1017HV4O	0	0
ASF1017HV	ASF1017HV5O	0	0
ASF1017HV	ASF1017HV6O	0	0
ASF1017HV	ASF1017HV7O	0	0
ASF1017HV	ASF1017HV8O	0	0
ASF1017HV	ASF1017HV9O	0	0
ASF1017HV	ASF1017HV10O	0	0
ASF1017HV	ASF1017HV11O	0	0
ASF1020HV	ASF1020HV1O	0	0
ASF1020HV	ASF1020HV2O	0	0
ASF1020HV	ASF1020HV3O	0	0
ASF1022HV	ASF1022HV1O	0	0
ASF1025HV	ASF1025HV1O	0	0
ASF1025HV	ASF1025HV2O	0	0
ASF1025HV	ASF1025HV3O	0	0
ASF1025HV	ASF1025HV4O	0	0
ASF1025HV	ASF1025HV5O	0	0
ASF1028HV	ASF1028HV1R	0	0
ASF1028HV	ASF1028HV2O	0	0
ASF1028HV	ASF1028HV3O	0	0
ASF1028HV	ASF1028HV4O	0	0
ASF1028HV	ASF1028HV5O	0	0
ASF1029HV	ASF1029HV1O	0	0
ASF1029HV	ASF1029HV2O	0	0
ASF1029HV	ASF1029HV3O	0	0
ASF1029HV	ASF1029HV4O	0	0
ASF1030HV	ASF1030HV1R	0	0
ASF1030HV	ASF1030HV2R	0	0
ASF1030HV	ASF1030HV3R	0	0
ASF1030HV	ASF1030HV4R	0	0
ASF1030HV	ASF1030HV5R	0	0

ID	TASRID	passed stool	burped
ASF1030HV	ASF1030HV6R	0	0
ASF1030HV	ASF1030HV7R	0	0
ASF1030HV	ASF1030HV8R	0	0
ASF1030HV	ASF1030HV9R	0	0
ASF1030HV	ASF1030HV10R	0	0
ASF1030HV	ASF1030HV11R	0	0
ASF1030HV	ASF1030HV12O	0	0
ASF1030HV	ASF1030HV13O	0	0
ASF1030HV	ASF1030HV14O	0	0
ASF1030HV	ASF1030HV15O	0	0
ASF1030HV	ASF1030HV16O	0	0
ASF1030HV	ASF1030HV17O	0	0
ASF1030HV	ASF1030HV18O	0	0
ASF1030HV	ASF1030HV19O	0	0
ASF1030HV	ASF1030HV20O	0	0
ASF1030HV	ASF1030HV21O	0	0
ASF1030HV	ASF1030HV22O	0	0
ASF1030HV	ASF1030HV23O	0	0
ASF1030HV	ASF1030HV24O	0	0
ASF1030HV	ASF1030HV25O	0	0
ASF1031HV	ASF1031HV1R	0	0
ASF1031HV	ASF1031HV2R	0	0
ASF1031HV	ASF1031HV3O	0	0
ASF1031HV	ASF1031HV4O	0	0
ASF1031HV	ASF1031HV5O	0	0
ASF1032HV	ASF1032HV1R	0	0
ASF1032HV	ASF1032HV2R	0	0
ASF1032HV	ASF1032HV3R	0	0
ASF1032HV	ASF1032HV4O	0	0
ASF1032HV	ASF1032HV5O	0	0
ASF1032HV	ASF1032HV6O	0	0
ASF1032HV	ASF1032HV7O	0	0
ASF1032HV	ASF1032HV8O	0	0
ASF1032HV	ASF1032HV9O	0	0
ASF1032HV	ASF1032HV10O	0	0
ASF1032HV	ASF1032HV11O	0	0
ASF1033HV	ASF1033HV1R	0	0
ASF1033HV	ASF1033HV2R	0	0
ASF1033HV	ASF1033HV3R	0	0
ASF1033HV	ASF1033HV4R	0	0
ASF1033HV	ASF1033HV5O	0	0
ASF1033HV	ASF1033HV6O	0	0
ASF1037HV	ASF1037HV1O	0	0
ASF1037HV	ASF1037HV2R	0	0
ASF1037HV	ASF1037HV3R	0	0

ID	TASRID	passed stool	burped
ASF1008HV	ASF1008HV1R	0	0
ASF1008HV	ASF1008HV2R	0	0
ASF1008HV	ASF1008HV3R	0	0
ASF1008HV	ASF1008HV4R	0	0
ASF1008HV	ASF1008HV5R	0	0
ASF1008HV	ASF1008HV6R	0	0
ASF1008HV	ASF1008HV7R	0	0
ASF1008HV	ASF1008HV8O	0	0
ASF1008HV	ASF1008HV9O	0	0
ASF1008HV	ASF1008HV10O	0	0
ASF1008HV	ASF1008HV11O	0	0
ASF1008HV	ASF1008HV12O	0	0
ASF1008HV	ASF1008HV13O	0	0
ASF1008HV	ASF1008HV14O	0	0
ASF1008HV	ASF1008HV15O	0	0
ASF1008HV	ASF1008HV16O	0	0
ASF1008HV	ASF1008HV17O	0	0
ASF1008HV	ASF1008HV18O	0	0
ASF1023HV	ASF1023HV1O	0	0
ASF1023HV	ASF1023HV2R	0	0
ASF1023HV	ASF1023HV3R	0	0
ASF1023HV	ASF1023HV4R	0	0
ASF1023HV	ASF1023HV5R	0	0
ASF1023HV	ASF1023HV6R	0	0
ASF1023HV	ASF1023HV7R	0	0
ASF1023HV	ASF1023HV8R	0	0
ASF1023HV	ASF1023HV9R	0	0
ASF1023HV	ASF1023HV10R	0	0
ASF1002HV	ASF1002HV1R	0	0
ASF1002HV	ASF1002HV2R	0	0
ASF1002HV	ASF1002HV3O	0	0
ASF1002HV	ASF1002HV4O	0	0
ASF1002HV	ASF1002HV5O	0	0
ASF1002HV	ASF1002HV6O	0	0
ASF1002HV	ASF1002HV7O	0	0
ASF1002HV	ASF1002HV8O	0	0
ASF1002HV	ASF1002HV9O	0	0
ASF1002HV	ASF1002HV10O	0	0
ASF1002HV	ASF1002HV11O	0	0
ASF1002HV	ASF1002HV12O	0	0
ASF1002HV	ASF1002HV13O	0	0
ASF1002HV	ASF1002HV14O	0	0
ASF1002HV	ASF1002HV15O	0	0
ASF1002HV	ASF1002HV16O	0	0
ASF1002HV	ASF1002HV17O	0	0

ID	TASRID	passed stool	burped
ASF1002HV	ASF1002HV18O	0	0
ASF1002HV	ASF1002HV19O	0	0
ASF1002HV	ASF1002HV20O	0	0
ASF1002HV	ASF1002HV21O	0	0
ASF1002HV	ASF1002HV22O	0	0
ASF1002HV	ASF1002HV23O	0	0
ASF1002HV	ASF1002HV24O	0	0
ASF1002HV	ASF1002HV25O	0	0
ASF1002HV	ASF1002HV26O	0	0
ASF1002HV	ASF1002HV27O	0	0
ASF1002HV	ASF1002HV28O	0	0
ASF1002HV	ASF1002HV29O	0	0
ASF1002HV	ASF1002HV30O	0	0
ASF1002HV	ASF1002HV31O	0	0
ASF1002HV	ASF1002HV32O	0	0
ASF1002HV	ASF1002HV33O	0	0
ASF1002HV	ASF1002HV34O	0	0
ASF1002HV	ASF1002HV35O	0	0
ASF1002HV	ASF1002HV36O	0	0
ASF1002HV	ASF1002HV37O	0	0
ASF1002HV	ASF1002HV38O	0	0
ASF1002HV	ASF1002HV39O	0	0
ASF1002HV	ASF1002HV40O	0	0
ASF1002HV	ASF1002HV41O	0	0
ASF1002HV	ASF1002HV42O	0	0
ASF1002HV	ASF1002HV43O	0	0
ASF1002HV	ASF1002HV44O	0	0
ASF1002HV	ASF1002HV43O	0	0
ASF1002HV	ASF1002HV44O	0	0
ASF1002HV	ASF1002HV45O	0	0
ASF1002HV	ASF1002HV46O	0	0
ASF1002HV	ASF1002HV47O	0	0

ID	TASRID	
ASF1001HV	ASF1001HV1O	
ASF1001HV	ASF1001HV2O	TASRID
ASF1001HV	ASF1001HV3O	AC_length
ASF1001HV	ASF1001HV4O	Pre_time
ASF1001HV	ASF1001HV5O	Post_time
ASF1005HV	ASF1005HV1R	Ind_TASR_no
ASF1005HV	ASF1005HV2O	Pre_post
ASF1007HV	ASF1007HV1O	T_time
ASF1007HV	ASF1007HV2O	T_occurance
ASF1007HV	ASF1007HV3O	T_percept
ASF1007HV	ASF1007HV4O	percep_type
ASF1007HV	ASF1007HV5O	percep_intensity
ASF1010HV	ASF1010HV1R	duration
ASF1010HV	ASF1010HV2O	depth
ASF1010HV	ASF1010HV3O	depthPC
ASF1010HV	ASF1010HV4O	Rectal_press_before
ASF1010HV	ASF1010HV5O	Anal_press_before
ASF1010HV	ASF1010HV6O	T_rect_press
ASF1010HV	ASF1010HV7O	T_anal_press
ASF1011HV	ASF1011HV1R	T_anal_min_press
ASF1011HV	ASF1011HV2R	T_anal_change
ASF1011HV	ASF1011HV3O	T_analPCchange
ASF1012HV	ASF1012HV1R	T_rectal_change
ASF1013HV	ASF1013HV1O	T_rectalPCchange
ASF1013HV	ASF1013HV2O	T_wind
ASF1013HV	ASF1013HV3O	T_stool
ASF1014HV	ASF1014HV1R	
ASF1014HV	ASF1014HV2R	
ASF1014HV	ASF1014HV3R	
ASF1014HV	ASF1014HV4O	
ASF1014HV	ASF1014HV5O	
ASF1014HV	ASF1014HV6O	
ASF1014HV	ASF1014HV7O	
ASF1014HV	ASF1014HV8O	
ASF1014HV	ASF1014HV9O	
ASF1014HV	ASF1014HV10O	
ASF1014HV	ASF1014HV11O	
ASF1014HV	ASF1014HV12O	
ASF1014HV	ASF1014HV13O	
ASF1014HV	ASF1014HV14O	

ID	TASRID
ASF1014HV	ASF1014HV15O
ASF1014HV	ASF1014HV16O
ASF1014HV	ASF1014HV17O
ASF1014HV	ASF1014HV18O
ASF1014HV	ASF1014HV19O
ASF1014HV	ASF1014HV20O
ASF1014HV	ASF1014HV21O
ASF1014HV	ASF1014HV22O
ASF1014HV	ASF1014HV23O
ASF1014HV	ASF1014HV24O
ASF1014HV	ASF1014HV25O
ASF1017HV	ASF1017HV1R
ASF1017HV	ASF1017HV2O
ASF1017HV	ASF1017HV3O
ASF1017HV	ASF1017HV4O
ASF1017HV	ASF1017HV5O
ASF1017HV	ASF1017HV6O
ASF1017HV	ASF1017HV7O
ASF1017HV	ASF1017HV8O
ASF1017HV	ASF1017HV9O
ASF1017HV	ASF1017HV10O
ASF1017HV	ASF1017HV11O
ASF1020HV	ASF1020HV1O
ASF1020HV	ASF1020HV2O
ASF1020HV	ASF1020HV3O
ASF1022HV	ASF1022HV1O
ASF1025HV	ASF1025HV1O
ASF1025HV	ASF1025HV2O
ASF1025HV	ASF1025HV3O
ASF1025HV	ASF1025HV4O
ASF1025HV	ASF1025HV5O
ASF1028HV	ASF1028HV1R
ASF1028HV	ASF1028HV2O
ASF1028HV	ASF1028HV3O
ASF1028HV	ASF1028HV4O
ASF1028HV	ASF1028HV5O
ASF1029HV	ASF1029HV1O
ASF1029HV	ASF1029HV2O
ASF1029HV	ASF1029HV3O
ASF1029HV	ASF1029HV4O
ASF1030HV	ASF1030HV1R
ASF1030HV	ASF1030HV2R
ASF1030HV	ASF1030HV3R
ASF1030HV	ASF1030HV4R
ASF1030HV	ASF1030HV5R

ID	TASRID
ASF1030HV	ASF1030HV6R
ASF1030HV	ASF1030HV7R
ASF1030HV	ASF1030HV8R
ASF1030HV	ASF1030HV9R
ASF1030HV	ASF1030HV10R
ASF1030HV	ASF1030HV11R
ASF1030HV	ASF1030HV12O
ASF1030HV	ASF1030HV13O
ASF1030HV	ASF1030HV14O
ASF1030HV	ASF1030HV15O
ASF1030HV	ASF1030HV16O
ASF1030HV	ASF1030HV17O
ASF1030HV	ASF1030HV18O
ASF1030HV	ASF1030HV19O
ASF1030HV	ASF1030HV20O
ASF1030HV	ASF1030HV21O
ASF1030HV	ASF1030HV22O
ASF1030HV	ASF1030HV23O
ASF1030HV	ASF1030HV24O
ASF1030HV	ASF1030HV25O
ASF1031HV	ASF1031HV1R
ASF1031HV	ASF1031HV2R
ASF1031HV	ASF1031HV3O
ASF1031HV	ASF1031HV4O
ASF1031HV	ASF1031HV5O
ASF1032HV	ASF1032HV1R
ASF1032HV	ASF1032HV2R
ASF1032HV	ASF1032HV3R
ASF1032HV	ASF1032HV4O
ASF1032HV	ASF1032HV5O
ASF1032HV	ASF1032HV6O
ASF1032HV	ASF1032HV7O
ASF1032HV	ASF1032HV8O
ASF1032HV	ASF1032HV9O
ASF1032HV	ASF1032HV10O
ASF1032HV	ASF1032HV11O
ASF1033HV	ASF1033HV1R
ASF1033HV	ASF1033HV2R
ASF1033HV	ASF1033HV3R
ASF1033HV	ASF1033HV4R
ASF1033HV	ASF1033HV5O
ASF1033HV	ASF1033HV6O
ASF1037HV	ASF1037HV1O
ASF1037HV	ASF1037HV2R
ASF1037HV	ASF1037HV3R

ID	TASRID
ASF1008HV	ASF1008HV1R
ASF1008HV	ASF1008HV2R
ASF1008HV	ASF1008HV3R
ASF1008HV	ASF1008HV4R
ASF1008HV	ASF1008HV5R
ASF1008HV	ASF1008HV6R
ASF1008HV	ASF1008HV7R
ASF1008HV	ASF1008HV8O
ASF1008HV	ASF1008HV9O
ASF1008HV	ASF1008HV10O
ASF1008HV	ASF1008HV11O
ASF1008HV	ASF1008HV12O
ASF1008HV	ASF1008HV13O
ASF1008HV	ASF1008HV14O
ASF1008HV	ASF1008HV15O
ASF1008HV	ASF1008HV16O
ASF1008HV	ASF1008HV17O
ASF1008HV	ASF1008HV18O
ASF1023HV	ASF1023HV1O
ASF1023HV	ASF1023HV2R
ASF1023HV	ASF1023HV3R
ASF1023HV	ASF1023HV4R
ASF1023HV	ASF1023HV5R
ASF1023HV	ASF1023HV6R
ASF1023HV	ASF1023HV7R
ASF1023HV	ASF1023HV8R
ASF1023HV	ASF1023HV9R
ASF1023HV	ASF1023HV10R
ASF1002HV	ASF1002HV1R
ASF1002HV	ASF1002HV2R
ASF1002HV	ASF1002HV3O
ASF1002HV	ASF1002HV4O
ASF1002HV	ASF1002HV5O
ASF1002HV	ASF1002HV6O
ASF1002HV	ASF1002HV7O
ASF1002HV	ASF1002HV8O
ASF1002HV	ASF1002HV9O
ASF1002HV	ASF1002HV10O
ASF1002HV	ASF1002HV11O
ASF1002HV	ASF1002HV12O
ASF1002HV	ASF1002HV13O
ASF1002HV	ASF1002HV14O
ASF1002HV	ASF1002HV15O
ASF1002HV	ASF1002HV16O
ASF1002HV	ASF1002HV17O

ID	TASRID
ASF1002HV	ASF1002HV18O
ASF1002HV	ASF1002HV19O
ASF1002HV	ASF1002HV20O
ASF1002HV	ASF1002HV21O
ASF1002HV	ASF1002HV22O
ASF1002HV	ASF1002HV23O
ASF1002HV	ASF1002HV24O
ASF1002HV	ASF1002HV25O
ASF1002HV	ASF1002HV26O
ASF1002HV	ASF1002HV27O
ASF1002HV	ASF1002HV28O
ASF1002HV	ASF1002HV29O
ASF1002HV	ASF1002HV30O
ASF1002HV	ASF1002HV31O
ASF1002HV	ASF1002HV32O
ASF1002HV	ASF1002HV33O
ASF1002HV	ASF1002HV34O
ASF1002HV	ASF1002HV35O
ASF1002HV	ASF1002HV36O
ASF1002HV	ASF1002HV37O
ASF1002HV	ASF1002HV38O
ASF1002HV	ASF1002HV39O
ASF1002HV	ASF1002HV40O
ASF1002HV	ASF1002HV41O
ASF1002HV	ASF1002HV42O
ASF1002HV	ASF1002HV43O
ASF1002HV	ASF1002HV44O
ASF1002HV	ASF1002HV43O
ASF1002HV	ASF1002HV44O
ASF1002HV	ASF1002HV45O
ASF1002HV	ASF1002HV46O
ASF1002HV	ASF1002HV47O

ID	vaginal number	caesarian number	instruments	episiotomy	tear
ASF1001A	5	0	0	0	3
ASF1002A	3	0	1	1	1
ASF1003A	2	0	0	2	1
ASF1004A	1	0	0	0	0
ASF1005A	3	0	2	3	2
ASF1007A	4	0	0	0	1
ASF1011A	3	0	1	1	1
ASF1012A	3	0	0	0	1
ASF1013A	3	1	1	1	1
ASF1015A	2	0	0	0	1

ID	menopause	hysterectomy	urge	passive	duration	anal surgery
ASF1001A	1	1	1	1	3	0
ASF1002A	1	0	1	1	5	0
ASF1003A	1	0	1	1	1	0
ASF1004A	0	0	1	0	1	1
ASF1005A	1	1	1	1	5	0
ASF1007A	1	1	1	1	15	0
ASF1011A	1	1	1	1	2	0
ASF1012A	1	1	1	1	10	0
ASF1013A	1	1	0	1	2	0
ASF1015A	1	1	1	0	1	0

ID	cat	sex	age	parous	anal_sens	FCS	DDV	MTV	Vaizey	CC_score
ASF1001A	1	0	49	1	32.93	160	240	300	20	7
ASF1002A	1	0	65	1	24.80	45	120	180	13	0
ASF1003A	1	0	65	1	7.87	50	105	108	11	4
ASF1004A	1	0	28	1	4.80	35	100	160	8	8
ASF1005A	1	0	77	1	11.20	100	245	340	10	3
ASF1006A	1	1	43	3	7.60	60	120	180	22	0
ASF1007A	1	0	49	1	8.80	120	180	235	15	13
ASF1009A	1	1	47	3	8.20	35	153	217	17	0
ASF1010A	1	1	44	3	28.47	140	190	284	19	7
ASF1011A	1	0	72	1	10.93	23	95	138	17	8
ASF1012A	1	0	70	1	12.87	24	68	144	16	5
ASF1013A	1	0	60	1	15.53	82	130	170	14	1
ASF1014A	1	0	59	0	7.60	40	107	177	16	1
ASF1016A	1	1	45	3	15.47	40	120	240	16	6

ID	PAC_SYM	FACL	HRAM_rest	profile_rest	HRAM_ave_squeeze	profile_squeeze
ASF1001A	27	2.9	88	175.45	6	179.8
ASF1002A	7	4.4	54	170.72	35	198
ASF1003A	9	3.4	36	85	62	127.5
ASF1004A	7	3.8	70	182.4	318	1022.2
ASF1005A	3	1.5	22	27	3	45
ASF1006A	0	3.2	83	179.2	5	172.8
ASF1007A	30	3.4	18	49.5	27	148.5
ASF1009A	5	5.1	84	300.9	104	741
ASF1010A	24	4.3	80	240.8	57	480.6
ASF1011A	13	4.4	72	140.8	5	160
ASF1012A	1	4.2	90	277.2	16	355.5
ASF1013A	5	2.8	54	106.4	13	92.4
ASF1014A	0	2.9	61	107.3	95	379.6
ASF1016A	16	5.5	83	286	43	528

ID	Pre_TASR	Pre_felt_TASR	Post_TASR	Post_felt_TASR	TASR_difference	Total_TASR
ASF1001A	0	0	0	0	0	0
ASF1002A	0	0	1	0	1	1
ASF1003A	0	0	1	0	1	1
ASF1004A	0	0	0	0	0	0
ASF1005A	0	0	2	0	2	2
ASF1006A	0	0	1	0	1	1
ASF1007A	1	1	0	0	-1	1
ASF1009A	0	0	0	0	0	0
ASF1010A	1	1	0	0	-1	0
ASF1011A	0	0	3	0	3	0
ASF1012A	2	2	0	0	2	0
ASF1013A	0	0	0	0	0	0
ASF1014A	0	0	5	1	5	5
ASF1016A	0	0	0	0	0	0

TASRID	AC_length	Pre_post	T_time	T_percept	percep_type	percep_inter
ASF1002A1	2.7	O		0	0	0
ASF1003A1	3.2	O		0	0	0
ASF1005A1	2.6	O	01:56:01	0	0	0
ASF1005A2	2.6	O	02:07:11	0	0	0
ASF1007A1	3.3	P	0:45:00	0	0	0
ASF1011A1	3.8	O	02:19:01	0	0	0
ASF1011A2	3.8	O	02:20:34	0	0	0
ASF1011A3	3.8	O	02:21:35	0	0	0
ASF1012A1	3.8	P	00:39:10	1	1	2.1
ASF1012A1	3.8	P	00:49:30	1	1	1.9

TASRID	duration	depth	depthPC	Rectal_press_before	Anal_press_before
ASF1002A1	54	1.8	66.7	38.8	56.8
ASF1003A1	47	1.8	56.3	33.5	68.5
ASF1005A1	143	2.6	100.0	28.8	44.3
ASF1005A2	68	2.6	100.0	30.3	42.5
ASF1007A1	12	3.3	100.0	27.7	61.0
ASF1011A1	25	1.6	42.1	31.0	83.3
ASF1011A2	19	1.6	42.1	31.5	83.7
ASF1011A3	20	1.6	42.1	35.0	80.8
ASF1012A1	30	1.1	28.9	30.3	75.7
ASF1012A1	27	1.1	28.9	33.0	78.0

TASRID	T_rect_press	T_anal_press	T_anal_min_press	T_anal_change	T_analPCchange
ASF1002A1	38.3	42.3	28	-15	-25.55
ASF1003A1	30.0	49.0	40	-20	-28.47
ASF1005A1	32.5	34.5	33	-10	-22.03
ASF1005A2	31.5	36.3	35	-6	-14.71
ASF1007A1	22.7	24.5	25	-37	-59.84
ASF1011A1	37.5	63.5	43	-20	-23.80
ASF1011A2	36.3	65.8	65.75	-18	-21.41
ASF1011A3	35.5	62.5	41	-18	-22.60
ASF1012A1	36.3	49.7	39	-26	-34.36
ASF1012A1	41.3	51.0	38	-27	-34.62

TASRID	T_rectal_change	T_rectalPCchange	T_wind	T_stool
ASF1002A1	-0.50	-1.29	0	0
ASF1003A1	-3.50	-10.45	0	0
ASF1005A1	3.75	13.04	0	0
ASF1005A2	1.25	4.13	0	0
ASF1007A1	-5.00	-18.07	0	0
ASF1011A1	6.50	20.97	0	0
ASF1011A2	4.83	15.34	0	0
ASF1011A3	0.50	1.43	0	0
ASF1012A1	5.92	19.51	0	0
ASF1012A1	8.33	25.25	0	0

Appendix C – study documents

Study ID: Date:

Cleaning record:

☐ Probe cleaned as per SOP

Tristel identification sticker

Scope check result ___________________

Anal sensorimotor function exclusion criteria

☐ Normal anorectal function as ascertained via clinical history

☐ No history of neurological disorders

☐ No use of medications that could potentially influence anal function

☐ No history of anorectal surgery or trauma

☐ Ability to provide informed consent for the study

☐ Ability to communicate effectively in English

Signed: ______________________________ Researcher name: ________________________

Date ____ / _____ / ______

HRAM History Sheet

Demographics

Study number	______________________	Date	______________________
Height	______________________	Weight	______________________
Sex	______________________	Ethnicity	______________________
Ethnic category code	______________________	Age	______________________

Past medical history

Condition	Date of diagnosis	Treatment
________________	_______________________	____
________________	_______________________	____
________________	_______________________	____
________________	_______________________	____
________________	_______________________	____
________________	_______________________	____
________________	_______________________	____

Obstetric history

Year	mode of delivery	Instruments	Episiotomy	Tear
________	________________	_________________	_______________	__________
________	________________	_________________	_______________	__________
________	________________	_________________	_______________	__________
________	________________	_________________	_______________	__________
________	________________	_________________	_______________	__________

Menopause

Pre Post

Medications

Name	dose
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________

Surgical history

Procedure	year
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________
___________________________________	_____________________

Bowel function

Frequency	______________	per day / week / month
Consistency	______________	as per bristol stool chart
Defer defaecation	______________	minute(s)
Time on pan	______________	minute(s)
Straining	__________________________	Pain ____________________
Manual manoeuvres	____	
Unsuccessful	____	
Incomplete	____	

Laxatives/ enemas/ suppositories	1. _________________________	4. _________________________
	2. _________________________	5. _________________________
	3. _________________________	6. _________________________

Passive incontinence	______________	duration in months / years
	______________	per day / week / month
	______________	small / medium / large
	______________	solid / liquid
Urge incontinence	______________	duration in months / years
	______________	per day / week / month
	______________	small / medium / large
	______________	solid / liquid
Abdominal pain	______________	duration in months / years
	______________	per day / week / month

Cleveland clinic score (to be filled in by researcher)

1. Frequency of bowel movements

0	1-2 times per 1-2 days
1	2 times per week
2	Once per week
3	Less than once per week
4	Less than once per month

2. Difficulty: painful evacuation effort

0	Never
1	Rarely
2	Sometimes
3	Usually
4	Always

3. Completeness: feeling incomplete evacuation

0	Never
1	Rarely
2	Sometimes
3	Usually
4	Always

4. Pain: Abdominal pain

0	Never
1	Rarely
2	Sometimes
3	Usually
4	Always

5. Minutes in lavatory per attempt

0	Less than 5
1	5-10
2	10-20
3	20-30
4	More than 30

6. Assistance: Type of assistance

0	Without assistance
1	Stimulative laxatives
2	Digital assistance or enema

7. Unsuccessful attempts for evacuation per 24 hours

0	Never
1	1-2
2	3-6
3	6-9
4	More than 9

8. Duration of constipation (in years)

0	0
1	1-5
2	5-10
3	10-20
4	More than 20

Results Sheet

Examination findings

Clinical evidence of dyssynergia: Yes / No

tick if performed

High Resolution anorectal manometry

Familiarisation	__
Resting	__
Squeeze	__
Endurance Squeeze	__
Push	__
Cough	__
RAIR	__
Rectal sensation	__

Anal sensitivity to electrical stimulation __

Frequency 5Hz, pulse width 0.1 ms

1cm Threshold 1:

Threshold 2:

Threshold 3:

2cm Threshold 1:

Threshold 2:

Threshold 3:

3cm Threshold 1:

Threshold 2:

Threshold 3:

ASF study

Sensation booklet

Female

Version 1: 19/02/2013

Preprandial

Study number

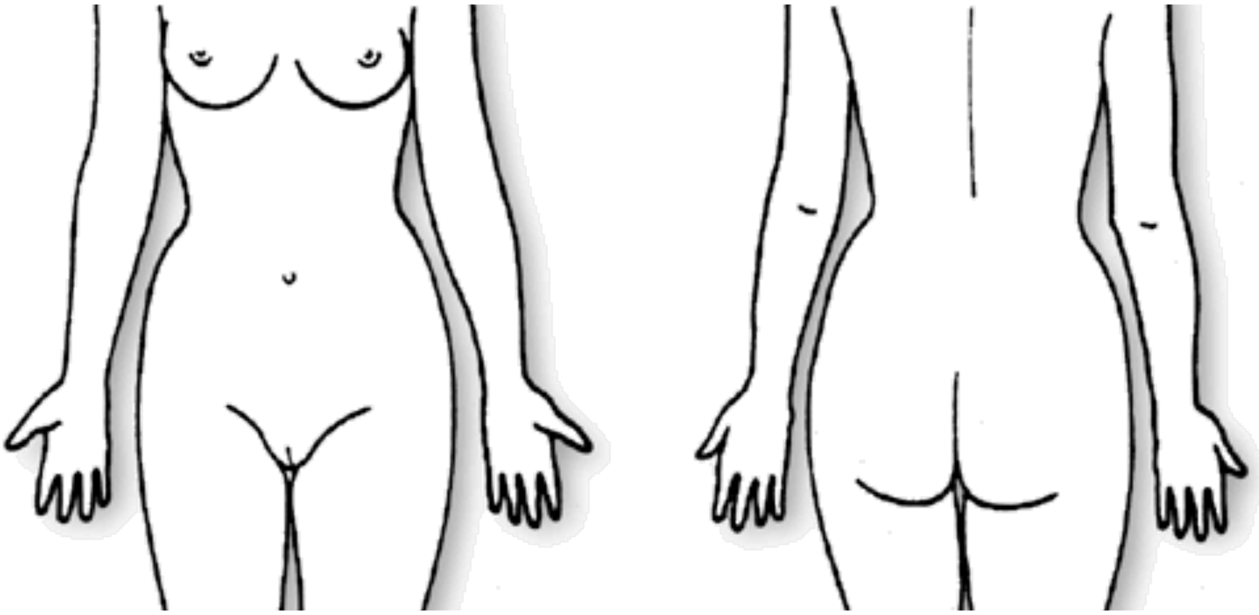
Date

Booklet of

Investigator

Beore we start the next part of the experiment please complete the following questions by circling the most appropriate answer

Event number: Event time:



No feeling at all

Strongest feeling imaginable

What type of feeling was this?

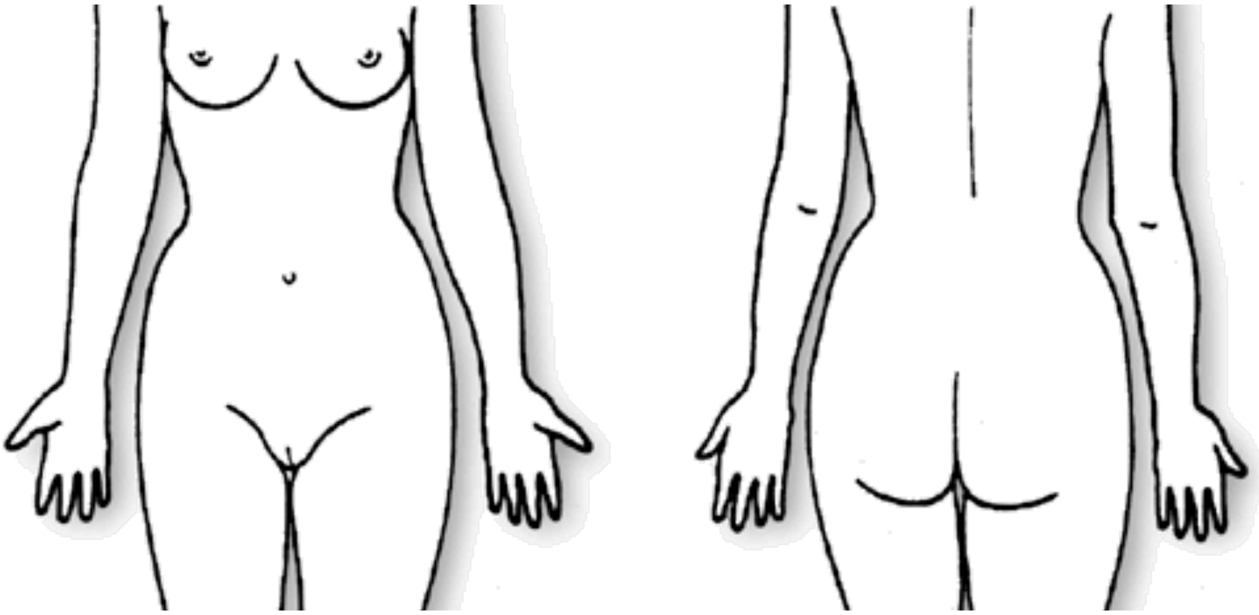
- ○ Urge to pass wind
- ○ Urge to pass stool
- ○ Tummy rumbling
- ○ Abdominal pain
- ○ Burp
- ○ Other

How would you describe this feeling? Please tick *any* applicable words below or add your own

- ☐ Aching
- ☐ Bloating
- ☐ Butterflies/gurgling
- ☐ Colicky/griping
- ☐ Cramping
- ☐ Fullness
- ☐ Heat/burning
- ☐ Heaviness/dragging
- ☐ Irritation
- ☐ Pressure
- ☐ Prickling
- ☐ Sickness/nausea
- ☐ Spasm
- ☐ Squeezing
- ☐ Stabbing
- ☐ Throbbing
- ☐ Tickling
- ☐ Tingling
- ☐ I can't describe the feeling

☐ Other - please describe:

Event number: Event time:



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How would you describe this feeling? Please tick *any* applicable words below or add your own

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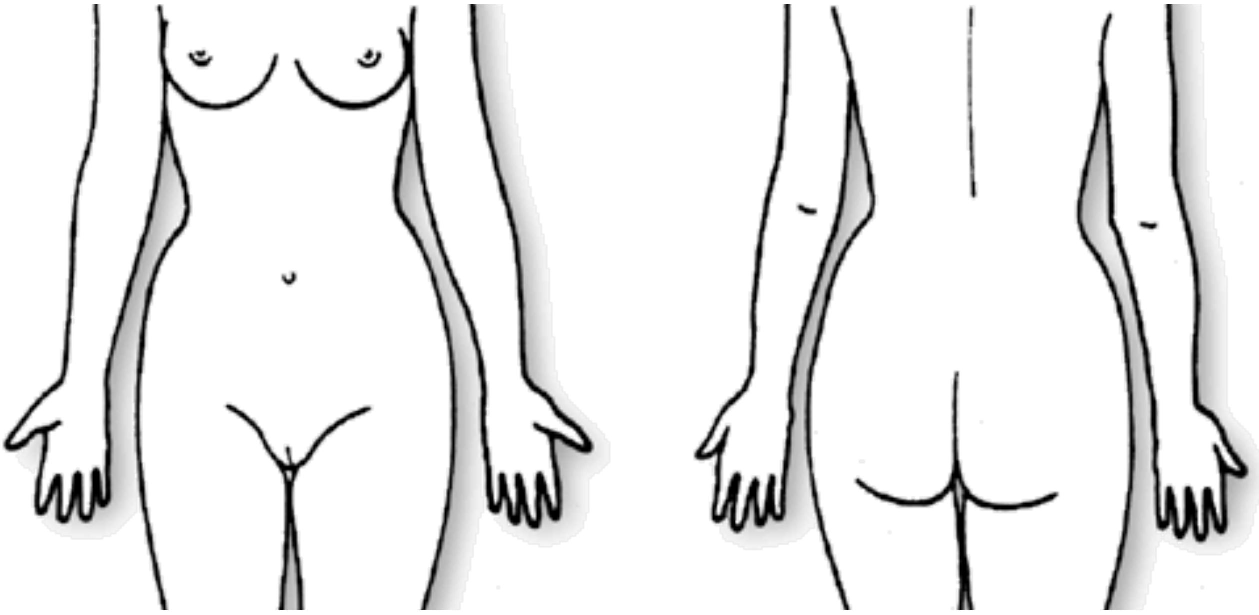
☐ Bloating	☐ Heat/burning	☐ Sickness/nausea	☐ Tickling
☐ Butterflies/gurgling	☐ Heaviness/dragging	☐ Spasm	☐ Tingling
☐ Colicky/griping	☐ Irritation	☐ Squeezing	☐ I can't describe the feeling
☐ Cramping	☐ Pressure	☐ Stabbing	

☐ Other - please describe:

Event number: Event time:



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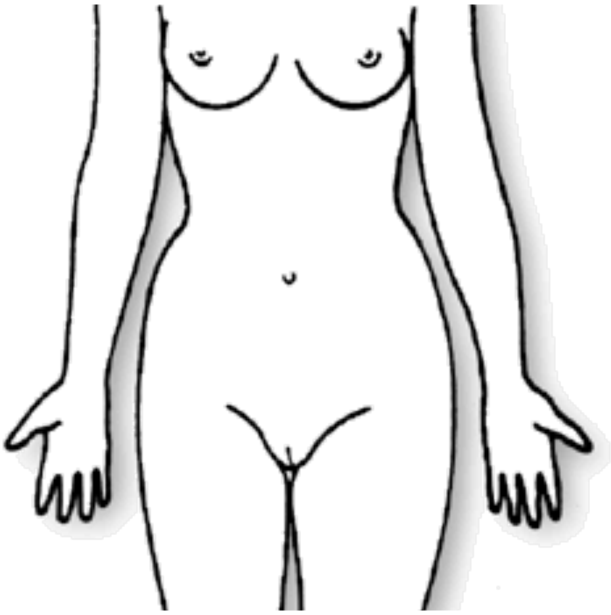
☐ Butterflies/gurgling	☐ Heaviness/dragging	☐ Spasm	☐ Tingling
☐ Colicky/griping	☐ Irritation	☐ Squeezing	☐ I can't describe the feeling
☐ Cramping	☐ Pressure	☐ Stabbing	

☐ Other - please describe:

Event number: Event time:



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- ☐ Squeezing
- ☐ Stabbing
- ☐ Throbbing
- ☐ Tickling
- ☐ Tingling
- ☐ I can't describe the feeling

☐ Other - please describe:

If you have come to the end of this booklet please ask the investigator for another one